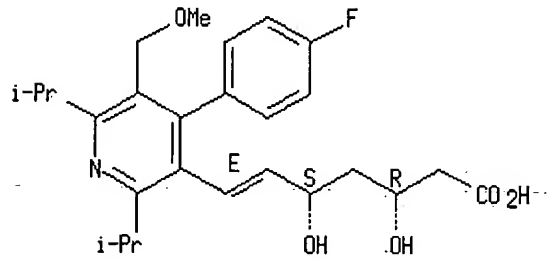
FILE 'HOME' ENTERED AT 10:05:37 ON 04 DEC 2001

=> fil reg
=> s lovastatin/cn or simvastatin/cn or atorvastatin/cn or cerivastatin/cn
             1 LOVASTATIN/CN
             1 SIMVASTATIN/CN
             1 ATORVASTATIN/CN
             1 CERIVASTATIN/CN
L1   4 LOVASTATIN/CN OR SIMVASTATIN/CN OR ATORVASTATIN/CN OR CERIVASTAT
               IN/CN

=> d tot

L1   ANSWER 1 OF 4 REGISTRY COPYRIGHT 2001 ACS
RN   145599-86-6 REGISTRY
CN   6-Heptenoic acid, 7-[4-(4-fluorophenyl)-5-(methoxymethyl)-2,6-bis(1-
     methylethyl)-3-pyridinyl]-3,5-dihydroxy-, (3R,5S,6E)- (9CI) (CA INDEX
     NAME)
OTHER CA INDEX NAMES:
CN   6-Heptenoic acid, 7-[4-(4-fluorophenyl)-5-(methoxymethyl)-2,6-bis(1-
     methylethyl)-3-pyridinyl]-3,5-dihydroxy-, [S-[R*,S*-(E)]]-
OTHER NAMES:
CN   (3R,5S,6E)-7-[4-(p-Fluorophenyl)-2,6-diisopropyl-5-(methoxymethyl)-3-
     pyridyl]-3,5-dihydroxy-6-heptenoic acid
CN   **Cerivastatin**
FS   STEREOSEARCH
MF   C26 H34 F N O5
CI   COM
SR   World Health Organization
LC   STN Files: ADISINSIGHT, ADISNEWS, BIOBUSINESS, BIOSIS, CA, CAPLUS, CBNB,
       CEN, CHEMCATS, CIN, CSNB, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES,
       IPA, MRCK*, PROMT, SYNTHLINE, TOXCENTER, TOXLIT, USAN, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources: WHO

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



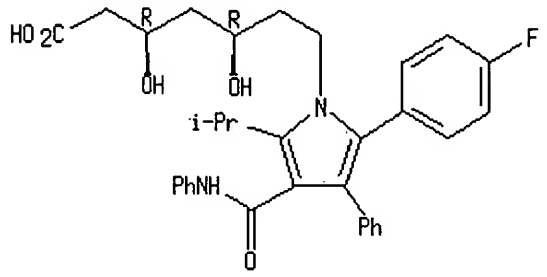
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

           195 REFERENCES IN FILE CA (1967 TO DATE)
             8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
           196 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1   ANSWER 2 OF 4 REGISTRY COPYRIGHT 2001 ACS
RN   134523-00-5 REGISTRY
CN   1H-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)-β,δ-dihydroxy-5-
     (1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-, (βR,δR)-
     (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)-β,δ-dihydroxy-5-
     (1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-, [R-(R*,R*)]-
OTHER NAMES:
CN   (βR,δR)-2-(p-Fluorophenyl)-β,δ-dihydroxy-5-isopropyl-
     3-phenyl-4-(phenylcarbamoyl)pyrrole-1-heptanoic acid
CN   **Atorvastatin**
FS   STEREOSEARCH
MF   C33 H35 F N2 O5

CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CBNB, CEN, CHEMCATS, CIN, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHARMASEARCH, PROMT, SYNTHLINE, TOXCENTER, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.

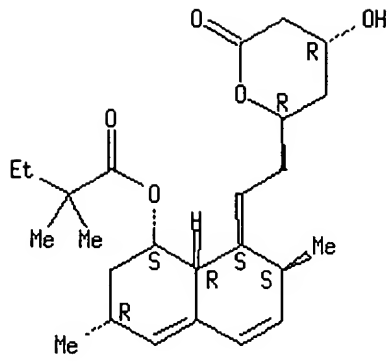


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

394 REFERENCES IN FILE CA (1967 TO DATE)
15 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
396 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2001 ACS
RN 79902-63-9 REGISTRY
CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Butanoic acid, 2,2-dimethyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1α,3α,7β,8β(2S*,4S*),8aβ]]-
OTHER NAMES:
CN (+)-Simvastatin
CN L 644128-000U
CN MK 733
CN **Simvastatin**
CN Synvinolin
CN Velostatin
CN Zocor
FS STEREOSEARCH
DR 98609-43-9, 118607-03-7
MF C25 H38 O5
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, PHAR, PHARMASEARCH, PROMT, RTECS*, SYNTHLINE, TOXCENTER, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.

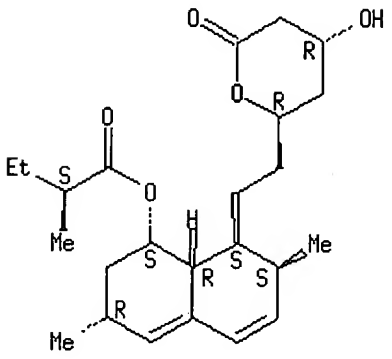


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1076 REFERENCES IN FILE CA (1967 TO DATE)
18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1080 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2001 ACS
RN 75330-75-5 REGISTRY
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1α(R*),3α,7β,8β(2S*,4S*),8aβ]]-
OTHER NAMES:
CN (+)-Mevinolin
CN Antibiotic MB 530B
CN L 154803
CN **Lovastatin**
CN Mevacor
CN Mevinolin
CN MK 803
CN Monacolin K
CN Monacolin K lactone
CN MSD 803
FS STEREOSEARCH
DR 71949-96-7, 74133-25-8, 81739-26-6
MF C24 H36 O5
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.



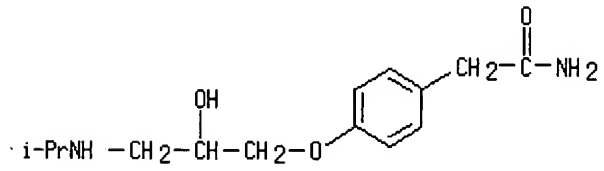
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1422 REFERENCES IN FILE CA (1967 TO DATE)
51 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1421 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> s propranolol/cn or atenolol/cn
1 PROPRANOLOL/CN
1 ATENOLOL/CN
L2 2 PROPRANOLOL/CN OR ATENOLOL/CN

=> d tot

L2 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2001 ACS
RN 29122-68-7 REGISTRY
CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Acetamide, 2-[p-[2-hydroxy-3-(isopropylamino)propoxy]phenyl]- (8CI)
OTHER NAMES:
CN (±)-Atenolol
CN (RS)-Atenolol
CN **Atenolol**
CN dl-Atenolol
CN DL-Atenolol
CN Duraatenolol
CN ICI 66082
CN Tenormin
FS 3D CONCORD
DR 106020-65-9, 60966-51-0
MF C14 H22 N2 O3
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGPAT, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

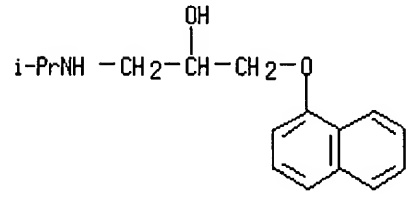


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2250 REFERENCES IN FILE CA (1967 TO DATE)
14 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2256 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2001 ACS
RN 525-66-6 REGISTRY
CN 2-Propanol, 1-[(1-methylethyl)amino]-3-(1-naphthalenyloxy)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Propanol, 1-(isopropylamino)-3-(1-naphthyloxy)- (7CI, 8CI)
OTHER NAMES:
CN (±)-Propranolol
CN β-Propranolol
CN 1-(1-Naphthyloxy)-3-(isopropylamino)-2-propanol

CN 1-(Isopropylamino)-3-(1-naphthyloxy)-2-propanol
CN AY 64043
CN Betalong
CN DL-Propranolol
CN dl-Propranolol
CN **Propranolol**
CN Proprasylyt
CN Racemic propranolol
CN Reducor
FS 3D CONCORD
DR 13013-17-7
MF C16 H21 N O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
    BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,
    CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSNB, DDFU, DIOGENES, DRUGPAT,
    DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*,
    NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, TOXCENTER,
    TOXLIT, ULIDAT, USAN, USPATFULL, VETU
      (*File contains numerically searchable property data)
    Other Sources: EINECS**, WHO
      (**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8896 REFERENCES IN FILE CA (1967 TO DATE)
102 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8903 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> fil medl capl biosis uspatfu;

=> s l1 or lovastatin or simvastatin or atorvastatin or cerivastatin
L3 13047 L1 OR LOVASTATIN OR SIMVASTATIN OR ATORVASTATIN OR CERIVASTATIN

=> s l2 or propranolol or atenolol or metoprolol
L4 118401 L2 OR PROPRANOLOL OR ATENOLOL OR METOPROLOL

=> s l3 and l4
L5 216 L3 AND L4

=> s l3 (s) l4
L6 103 L3 (S) L4

=> dup rem l6; focus
PROCESSING COMPLETED FOR L6
L7 96 DUP REM L6 (7 DUPLICATES REMOVED)

PROCESSING COMPLETED FOR L7
L8 96 FOCUS L7 1-

=> d ibib abs kwic 1-5

L8 ANSWER 1 OF 96 MEDLINE
Full-text
ACCESSION NUMBER: 91329151 MEDLINE
DOCUMENT NUMBER: 91329151 PubMed ID: 1907839
TITLE: Pharmacokinetic interaction between **propranolol** and the HMG-CoA reductase inhibitors pravastatin and **lovastatin**.
AUTHOR: Pan H Y; Triscari J; DeVault A R; Smith S A; Wang-Iverson D; Swanson B N; Willard D A

CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, New Brunswick, NJ.
SOURCE: BRITISH JOURNAL OF CLINICAL PHARMACOLOGY, (1991 Jun) 31 (6) 665-70.
Journal code: AU9; 7503323. ISSN: 0306-5251.
PUB. COUNTRY: ENGLAND: United Kingdom
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199109
ENTRY DATE: Entered STN: 19911006
Last Updated on STN: 19950206
Entered Medline: 19910913

AB 1. Single oral 20 mg doses of the HMG-CoA reductase inhibitors pravastatin and **lovastatin**, with and without concomitant **propranolol** (40 mg twice daily), were administered to 16 healthy male subjects participating in a randomized, four-way crossover study. 2. Serum concentrations of total and active inhibitors were measured by bioassay and concentrations of pravastatin, two pravastatin metabolites and **lovastatin** acid were measured by gas chromatography/mass spectrometry. 3. Coadministration of **propranolol** with pravastatin reduced the mean area under the serum concentration-time curve (AUC) of total inhibitors by 23%, of active inhibitors by 20% and of pravastatin by 16%. 4. Coadministration of **propranolol** with **lovastatin** also resulted in decreases in the mean serum AUC of total inhibitors by 18%, of active inhibitors by 12% and of **lovastatin** acid by 13%. 5. These decreases in systemic drug concentrations may reflect enhanced drug first-pass hepatic clearance in the presence of **propranolol**. 6. The clinical significance of these changes is likely to be small.

TI Pharmacokinetic interaction between **propranolol** and the HMG-CoA reductase inhibitors pravastatin and **lovastatin**.

AB 1. Single oral 20 mg doses of the HMG-CoA reductase inhibitors pravastatin and **lovastatin**, with and without concomitant **propranolol** (40 mg twice daily), were administered to 16 healthy male subjects participating in a randomized, four-way crossover study. 2. Serum concentrations of total and active inhibitors were measured by bioassay and concentrations of pravastatin, two pravastatin metabolites and **lovastatin** acid were measured by gas chromatography/mass spectrometry. 3. Coadministration of **propranolol** with pravastatin reduced the mean area under the serum concentration-time curve (AUC) of total inhibitors by 23%, of active inhibitors by 20% and of pravastatin by 16%. 4. Coadministration of **propranolol** with **lovastatin** also resulted in decreases in the mean serum AUC of total inhibitors by 18%, of active inhibitors by 12% and of **lovastatin** acid by 13%. 5. These decreases in systemic drug concentrations may reflect enhanced drug first-pass hepatic clearance in the presence of **propranolol**. 6. The clinical significance of these changes is likely to be small.

L8 ANSWER 2 OF 96 MEDLINE
Full-text
ACCESSION NUMBER: 2001284884 MEDLINE
DOCUMENT NUMBER: 21068384 PubMed ID: 11156573
TITLE: Simvastatin inhibits noradrenaline-induced hypertrophy of cultured neonatal rat cardiomyocytes.
AUTHOR: Luo J D; Xie F; Zhang W W; Ma X D; Guan J X; Chen X
CORPORATE SOURCE: Department of Pharmacology, Guangzhou Medical College, Guangzhou 510182, China. Central Laboratory, The First Military Medical University, Guangzhou 510000, China.. joluoa@public.guangzhou.gd.cn
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (2001 Jan) 132 (1) 159-64.
Journal code: B00; 7502536. ISSN: 0007-1188.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010524

AB 1. Oxidative mechanisms have been implicated in neonatal cardiomyocyte hypertrophy. We and others have shown that a HMG-CoA reductase inhibitor preserves endogenous antioxidant enzyme activity and inhibits cardiac hypertrophy in vivo. We therefore have examined whether noradrenaline (NA)

induces the generation of reactive oxygen species (ROS) during its induction of neonatal cardiomyocyte hypertrophy and whether **simvastatin**, a HMG-CoA reductase inhibitor, attenuates ROS production and thus NA-induced hypertrophy of cardiomyocytes. 2. NA increased the intracellular ROS levels in a concentration-dependent manner. This increase of ROS was significantly inhibited by **simvastatin** and catalase. Prazosin partially suppressed NA-induced increase of ROS and beating, while preincubation with both prazosin and **propranolol** completely abolished NA-evoked increase of ROS and beating. **Simvastatin** did not affect NA-induced increase of beating. 3. The NA-induced increase of protein content was partially suppressed by prazosin and completely abolished by preincubation with both prazosin and **propranolol**. **Simvastatin** inhibited the increase of NA-induced increase of RNA content and [(3)H]-leucine incorporation in a concentration-dependent manner. Mevalonic acid (MVA) reversed the inhibition of NA-induced RNA and protein increase by **simvastatin**. Catalase also inhibited the NA-induced increase of RNA and protein. 4. We conclude that the inhibitory effects of **simvastatin** on myocyte hypertrophy were associated with its antioxidant effects and inhibition of MVA-metabolism pathway in neonatal rat cardiomyocytes. NA-induced increases of intracellular ROS and cardiomyocyte hypertrophy requires both alpha and beta adrenoceptors activation in neonatal rat cardiomyocytes. The increases of ROS induced by NA is required for hypertrophy.

AB . . . whether noradrenaline (NA) induces the generation of reactive oxygen species (ROS) during its induction of neonatal cardiomyocyte hypertrophy and whether **simvastatin**, a HMG-CoA reductase inhibitor, attenuates ROS production and thus NA-induced hypertrophy of cardiomyocytes. 2. NA increased the intracellular ROS levels in a concentration-dependent manner. This increase of ROS was significantly inhibited by **simvastatin** and catalase. Prazosin partially suppressed NA-induced increase of ROS and beating, while preincubation with both prazosin and **propranolol** completely abolished NA-evoked increase of ROS and beating. **Simvastatin** did not affect NA-induced increase of beating. 3. The NA-induced increase of protein content was partially suppressed by prazosin and completely abolished by preincubation with both prazosin and **propranolol**. **Simvastatin** inhibited the increase of NA-induced increase of RNA content and [(3)H]-leucine incorporation in a concentration-dependent manner. Mevalonic acid (MVA) reversed the inhibition of NA-induced RNA and protein increase by **simvastatin**. Catalase also inhibited the NA-induced increase of RNA and protein. 4. We conclude that the inhibitory effects of **simvastatin** on myocyte hypertrophy were associated with its antioxidant effects and inhibition of MVA-metabolism pathway in neonatal rat cardiomyocytes. NA-induced increases. . .

L8 ANSWER 3 OF 96 MEDLINE

Full-text

ACCESSION NUMBER: 94258636 MEDLINE
DOCUMENT NUMBER: 94258636 PubMed ID: 8199978
TITLE: [Severe rhabdomyolysis in a patient receiving lovastatin, danazol, and doxycycline].
Rhabdomyolyse severe chez un patient recevant lovastatine, danazol et doxycycline.
AUTHOR: Dallaire M; Chamberland M
CORPORATE SOURCE: Departement de medecine interne, Centre hospitalier Rouyn-Noranda, Que.
SOURCE: CMAJ, (1994 Jun 15) 150 (12) 1991-4.
Journal code: CVV; 9711805. ISSN: 0820-3946.
PUB. COUNTRY: Canada
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940714
Last Updated on STN: 19980206
Entered Medline: 19940707

AB Combinations of **lovastatin** and other drugs have been reported to cause rhabdomyolysis and myoglobinuria. The authors report such a case in a 72-year-old man who had been receiving **atenolol**, acetylsalicylic acid (ASA), dipyridamole, **lovastatin**, danazol, prednisone and doxycycline. The ASA, **lovastatin** and danazol were discontinued. The symptoms resolved, and laboratory test results were normal within 2 weeks. **Lovastatin** was strongly suspected; danazol was the most likely potentiator by diminishing the metabolism of **lovastatin** and its metabolites in the liver or by having a direct toxic effect on the muscles.

L8 ANSWER 4 OF 96 USPATFULL
Full-text
ACCESSION NUMBER: 2001:212586 USPATFULL
TITLE: In vivo delivery methods and compositions
INVENTOR(S): Kensey, Kenneth R., Malvern, PA, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001044584	A1	20011122
APPLICATION INFO.:	US 2001-819924	A1	20010328 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-727950, filed on 1 Dec 2000, PENDING Continuation-in-part of Ser. No. US 2000-628401, filed on 1 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-501856, filed on 10 Feb 2000, PENDING Continuation-in-part of Ser. No. US 1999-439795, filed on 12 Nov 1999, PENDING Continuation-in-part of Ser. No. US 1997-919906, filed on 28 Aug 1997, GRANTED, Pat. No. US 6019735
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: CAESAR, RIVISE, BERNSTEIN,, COHEN & POKOTILOW, LTD., 12TH FLOOR, SEVEN PENN CENTER, 1635 MARKET STREET, PHILADELPHIA, PA, 19103-2212
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 19 Drawing Page(s)
LINE COUNT: 2120

AB Various methods are provided for determining and utilizing the viscosity of the circulating blood of a living being over a range of shear rates for diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as peripheral arterial disease in combination with administering to a living being at least one pharmaceutically acceptable agent. Agents pharmaceutically effective to regulate at least one of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream.

DETD . . . isosorbide mononitrate, isosorbide dinitrate, nitroglycerin, hydralazine, minoxidil, hydrochlorothiazide, chlorothiazide, indapamide, metolazone, furosemide, bumetanide, ethacrynic acid, torsemide, spironolactone, triamterene, acetazolamide, mannitol, **atenolol**, bisoprolol, pindolol, **metoprolol**, timolol, nadolol, propanolol, carvedilol, captopril, fosinopril, benazepril, lisinopril, enalapril, quinapril, losartan, valsartan, eprosartan, trandolapril, fenoldopam, ramipril, doxazosin, milrinone, benidipine, lemakalim,. . . barnidipine, lacidipine, bucindolol, azelnidipine, dofetilide, ibutilide, watanidipine, lercanidipine, landiolol, telmisartan, furnidipine, azimilide, CHF 1521, valsartan/hydrochlorothlazide, enalapril/nitrondipine, sotalol, arbutamine, olmesartan, conivaptan, **lovastatin**, **atorvastatin**, **cerivastatin**, **simvastatin**, fluvastatin, cholestyramine, colestipol, clofibrate, gemfibrozil, fenofibrate, pamaqueside, pitavastatin, phentermine, phendimetrazine, sibutramine, orlistat, aspirin, warfarin, enoxaparin, heparin, low molecular weight heparin,. . .

CLM What is claimed is:

. . . isosorbide mononitrate, isosorbide dinitrate, nitroglycerin, hydralazine, minoxidil, hydrochlorothiazide, chlorothiazide, indapamide, metolazone, furosemide, bumetanide, ethacrynic acid, torsemide, spironolactone, triamterene, acetazolamide, mannitol, **atenolol**, bisoprolol, pindolol, **metoprolol**, timolol, nadolol, propanolol, carvedilol, captopril, fosinopril, benazepril, lisinopril, enalapril, quinapril, losartan, valsartan, eprosartan, trandolapril, fenoldopam, ramipril, doxazosin, milrinone, benidipine, lemakalim,. . . barnidipine, lacidipine, bucindolol, azelnidipine, dofetilide, ibutilide, watanidipine, lercanidipine, landiolol, telmisartan, furnidipine, azimilide, CHF 1521, valsartan/hydrochlorothlazide, enalapril/nitrondipine, sotalol, arbutamine, olmesartan, conivaptan, **lovastatin**, **atorvastatin**, **cerivastatin**, **simvastatin**, fluvastatin, cholestyramine, colestipol, clofibrate, gemfibrozil, fenofibrate, pamaqueside, pitavastatin, phentermine, phendimetrazine,

sibutramine, orlistat, aspirin, warfarin, enoxaparin, heparin, low molecular weight heparin,. . .

L8 ANSWER 5 OF 96 MEDLINE
Full-text
ACCESSION NUMBER: 94256376 MEDLINE
DOCUMENT NUMBER: 94256376 PubMed ID: 8198018
TITLE: Clinical implications of the biopharmaceutical properties of fluvastatin.
AUTHOR: Deslypere J P
CORPORATE SOURCE: Department of Internal Medicine, University Hospital, Gent, Belgium.
SOURCE: AMERICAN JOURNAL OF CARDIOLOGY, (1994 May 26) 73 (14) 12D-17D.
Journal code: 3DQ; 0207277. ISSN: 0002-9149.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940707
Last Updated on STN: 19940707
Entered Medline: 19940629

AB Fluvastatin sodium (Lescol; Sandoz) the first entirely synthetic 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor studied, is structurally distinct from the other HMG-CoA reductase inhibitors currently available, all of which are fungal metabolites and analogues of compactin. Fluvastatin's distinct structure may be responsible for the biopharmaceutical properties that result in its low systemic exposure and, subsequently, low incidence of peripheral adverse events, such as headache and myositis. Fluvastatin is rapidly absorbed from the gastrointestinal tract; has a 30-minute half-life, the shortest of any currently available HMG-CoA reductase inhibitor (**lovastatin**, 15 hours; pravastatin, 2 hours; **simvastatin**, 15.6 hours); is highly selective for the liver, undergoing extensive first-pass metabolism; has no active circulating metabolites; and does not penetrate the blood-brain barrier, unlike **lovastatin** and **simvastatin**. The low systemic exposure suggests that the occurrence of peripheral adverse events, such as myositis, central nervous system effects, and drug-drug interactions, may be less than what is currently observed with other HMG-CoA reductase inhibitors. Neither niacin nor **propranolol** had an effect on fluvastatin plasma levels when combined with fluvastatin. In contrast to other HMG-CoA reductase inhibitors, fluvastatin in combination with niacin resulted in no instances of myositis or other serious adverse events. Although the interaction of fluvastatin with cholestyramine resulted in a lower rate and extent of fluvastatin bioavailability, this reduction had no impact on clinical efficacy. Fluvastatin administered to patients chronically receiving digoxin had no effect on the area under the curve (AUC) of digoxin compared with controls.(ABSTRACT TRUNCATED AT 250 WORDS)

=> d ibib abs kwic 6-10

L8 ANSWER 6 OF 96 CAPLUS COPYRIGHT 2001 ACS
Full-text
ACCESSION NUMBER: 2001:762853 CAPLUS
DOCUMENT NUMBER: 135:308923
TITLE: Formulation for the prevention of cardiovascular disease
INVENTOR(S): Wald, Nicholas J.; Law, Malcolm R.
PATENT ASSIGNEE(S): UK
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001076632	A1	20011018	WO 2001-GB1618	20010410

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,

LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-8791 A 20000410
GB 2001-548 A 20010109

AB A method for the prevention of cardiovascular disease is administration of a combination of active principals for use in the prevention of cardiovascular disease, notably ischemic heart disease (including heart attacks) and stroke among the general adult population. Compns. contain, e.g., hydrochlorothiazide, **atenolol**, and enalapril as blood pressure lowering agents, **atorvastatin** as a lipid-regulating agent, aspirin as a platelet function altering agent, and folic acid as a serum homocysteine lowering agent.

REFERENCE COUNT: 4

REFERENCE(S): (1) Neutel, J; AMERICAN JOURNAL OF HYPERTENSION 1999, V12(8 PT 2), P73S MEDLINE
(2) Rhymer, P; WO 9811896 A 1998 CAPLUS
(3) Squibb Bristol Myers Co; WO 9819690 A 1998 CAPLUS
(4) Tobert, J; WO 9738694 A 1997 CAPLUS

L8 ANSWER 7 OF 96 USPATFULL

Full-text

ACCESSION NUMBER: 2000:174799 USPATFULL

TITLE: Biodegradable polymers chain-extended by phosphates, compositions, articles and methods for making and using the same

INVENTOR(S): Mao, Hai-Quan, Towson, MD, United States
Leong, Kam W., Ellicott City, MD, United States
Zhao, Zhong, Baltimore, MD, United States
English, James P., Chelsea, AL, United States

PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., Baltimore, MD, United States (U.S. corporation)
Johns Hopkins University, Baltimore, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6166173		20001226
APPLICATION INFO.:	US 1998-53649		19980402 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1997-832217, filed on 3 Apr 1997, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Merriam, Andrew E. C.
NUMBER OF CLAIMS: 260
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 17 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 2164

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Biodegradable polymers are described comprising the recurring monomeric units shown in formula I or II: wherein X is --O-- or --NR'--, where R' is H or alkyl; L is a branched or straight chain aliphatic group having from 1-20 carbon atoms; M and M are each independently (1) a branched or straight chain aliphatic group having from 1-20 carbon atoms; or (2) a branched or straight chain, oxy-, carboxy- or amino-aliphatic group having from 1-20 carbon atoms; Y is --O--, --S-- or --NR'--, where R' is H or alkyl; R is H, alkyl, alkoxy, aryl, aryloxy, heterocyclic or heterocycloxy; the molar ratio of x:y is about 1; the molar ratio n:(x or y) is between about 200:1 and 1:200; and the molar ratio q:r is between about 1:99 and 99:1; wherein said biodegradable polymer is biocompatible before and upon biodegradat.

Processes for preparing the polymers, compositions containing the polymers and biologically active substances, articles useful for implantation or injection into the body fabricated from the compositions, and methods for controllably releasing biologically active substances using the polymers, are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . as pilocarpine; (32) cholinesterase inhibitor parasympathomimetics, such as pyridostigmine; (33) α-blocker sympatholytics, such as prazosin; (34) β-blocker sympatholytics,

such as **atenolol**; (35) adrenergic agonist sympathomimetics, such as albuterol and dobutamine; (36) cardiovascular agents, such as aspirin (ASA) (enteric coated ASA); (37) β-blocker antianginals, such as **atenolol** and **propranolol**; (38) calcium-channel blocker antianginals, such as nifedipine and verapamil; (39) nitrate antianginals, such as isosorbide dinitrate (ISDN); (40) cardiac glycoside. . . as digoxin; (41) class I antiarrhythmics, such as lidocaine, mexiletine, phenytoin, procainamide, and quinidine; (42) class II antiarrhythmics, such as **atenolol**, **metoprolol**, **propranolol**, and timolol; (43) class III antiarrhythmics, such as amiodarone; (44) class IV antiarrhythmics, such as diltiazem and verapamil; (45) α-blocker. . . such as prazosin; (46) angiotensin-converting enzyme inhibitor (ACE inhibitor) antihypertensives, such as captopril and enalapril; (47) β-blocker antihypertensives, such as **atenolol**, **metoprolol**, nadolol, and **propranolol**; (48) calcium-channel blocker antihypertensive agents, such as diltiazem and nifedipine; (49) central-acting adrenergic antihypertensives, such as clonidine and methyldopa; (50). . . such as gemfibrozil and probucol; (53) bile acid sequestrant antilipemics, such as cholestyramine; (54) HMG-CoA reductase inhibitor antilipemics, such as **lovastatin** and pravastatin; (55) inotropes, such as amrinone, dobutamine, and dopamine; (56) cardiac glycoside inotropes, such as digoxin; (57) thrombolytic agents,. . .

L8 ANSWER 8 OF 96 MEDLINE
Full-text
ACCESSION NUMBER: 2001569449 IN-PROCESS
DOCUMENT NUMBER: 21530697 PubMed ID: 11675864
TITLE: Nightmares and sleep disturbances with **simvastatin** and **metoprolol**.
AUTHOR: Boriani G; Biffi M; Strocchi E; Branzi A
SOURCE: ANNALS OF PHARMACOTHERAPY, (2001 Oct) 35 (10) 1292.
Journal code: BBX; 9203131. ISSN: 1060-0280.
PUB. COUNTRY: United States
Letter
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20011029
Last Updated on STN: 20011029
TI Nightmares and sleep disturbances with **simvastatin** and **metoprolol**.

L8 ANSWER 9 OF 96 MEDLINE
Full-text
ACCESSION NUMBER: 1998454162 MEDLINE
DOCUMENT NUMBER: 98454162 PubMed ID: 9780877
TITLE: In the past 12 to 18 months, my level of anxiety has increased significantly. I have been on **atenolol** and **simvastatin** (Zocor) for the past couple of years. Is there anything in these drugs that could cause this anxiety?.
AUTHOR: Lee T H
SOURCE: HARVARD HEART LETTER, (1998 Oct) 9 (2) 8.
Journal code: C2Z; 9425723. ISSN: 1051-5313.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: K
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981029
TI In the past 12 to 18 months, my level of anxiety has increased significantly. I have been on **atenolol** and **simvastatin** (Zocor) for the past couple of years. Is there anything in these drugs that could cause this anxiety?.

L8 ANSWER 10 OF 96 BIOSIS COPYRIGHT 2001 BIOSIS
Full-text
ACCESSION NUMBER: 2001:550112 BIOSIS
DOCUMENT NUMBER: PREV200100550112
TITLE: Nightmares and sleep disturbances with **simvastatin** and **metoprolol**.
AUTHOR(S): Boriani, Giuseppe (1); Biffi, Mauro; Strocchi, Enrico; Branzi, Angelo
CORPORATE SOURCE: (1) Policlinico S. Orsola, Institute of Cardiology, University of Bologna, Via Massarenti 9, 40138, Bologna:

cardiol@almadns.unibo.it Italy
SOURCE: Annals of Pharmacotherapy, (October, 2001) Vol. 35, No. 10, pp. 1292. print.
ISSN: 1060-0280.
DOCUMENT TYPE: Article; Letter
LANGUAGE: English
SUMMARY LANGUAGE: English
TI Nightmares and sleep disturbances with **simvastatin** and **metoprolol**.

=> d ibib abs kwic 11-15

L8 ANSWER 11 OF 96 BIOSIS COPYRIGHT 2001 BIOSIS
Full-text
ACCESSION NUMBER: 1999:131259 BIOSIS
DOCUMENT NUMBER: PREV199900131259
TITLE: Effects of hypolipemic therapy on the pharmacokinetics of propranolol.
AUTHOR(S): Wojcicki, Jerzy (1); Sterna, Rozalia; Sulzyc-Bielicka, Violetta; Gawronska-Szklarz, Barbara; Drozdzik, Marek; Musial, Heros David
CORPORATE SOURCE: (1) Dep. Pharamcol. Toxicol., Pomeranian Med. Acad., Powstancow Wlkp. 72, 70-111 Szczecin Poland
SOURCE: Current Therapeutic Research, (Jan., 1999) Vol. 60, No. 1, pp. 20-30.
ISSN: 0011-393X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The pharmacokinetics of **propranolol** was studied in 34 patients with hyperlipidemia before and after a 30-day course of hypolipemic therapy. Based on their diagnosis, the patients were separated into hypercholesterolemic, hypertriglyceridemic, and mixed-form hyperlipidemic groups. Pharmacokinetic studies were performed at the onset of the study and after 30 days of treatment with **lovastatin** (hypercholesterolemic and mixed-form hyperlipidemic patients) or bezafibrate (hypertriglyceridemic patients). **Propranolol** 80 mg was given orally as a single dose before and after hypolipemic therapy, and blood serum was sampled during the 24 hours after drug administration. Effective hypolipemic therapy has been shown to induce changes in the pharmacokinetics of **propranolol**, depending on the type of lipid metabolic disturbance. The most pronounced alterations, such as an increase in volume of distribution, were observed in patients with hypertriglyceridemia. Hypercholesterolemic therapy did not significantly affect the pharmacokinetics of **propranolol**.

L8 ANSWER 12 OF 96 USPATFULL
Full-text
ACCESSION NUMBER: 2001:214666 USPATFULL
TITLE: Biodegradable terephthalate polyester-poly (phosphate) polymers, compositions, articles, and methods for making and using the same
INVENTOR(S): Mao, Hai-Quan, Towson, MD, United States
Leong, Kam W., Ellicott City, MD, United States
Dang, Wenbin, Baltimore, MD, United States
Lo, Hungnan, Shaker Heights, OH, United States
Zhao, Zhong, Baltimore, MD, United States
Nowotnik, David P., Kingsville, MD, United States
English, James P., Chelsea, AL, United States
PATENT ASSIGNEE(S): Guilford Pharmaceuticals, Inc., Baltimore, MD, United States (U.S. corporation)
Johns Hopkins University, Baltimore, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6322797	B1	20011127
APPLICATION INFO.:	US 1998-53648		19980402 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1997-832215, filed on 3 Apr 1997, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Truong, Duc
LEGAL REPRESENTATIVE: Foley, Hoag & Eliot LLP
NUMBER OF CLAIMS: 126
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 19 Drawing Figure(s); 15 Drawing Page(s)

LINE COUNT: 1946

AB Biodegradable terephthalate polymers are described comprising the recurring monomeric units shown in formula I: ##STR1##

wherein R is a divalent organic moiety;

R' is an aliphatic, aromatic or heterocyclic residue;

x is ≥1; and

n is 0-5,000,

wherein the biodegradable polymer is biocompatible before and upon biodegradation.

Processes for preparing the polymers, compositions containing the polymers and biologically active substances, articles useful for implantation or injection into the body fabricated from the compositions, and methods for controllably releasing biologically active substances using the polymers, are also described.

DETD . . . as pilocarpine; (32) cholinesterase inhibitor parasympathomimetics, such as pyridostigmine; (33) α-blocker sympatholytics, such as prazosin; (34) 9-blocker sympatholytics, such as **atenolol**; (35) adrenergic agonist sympathomimetics, such as albuterol and dobutamine; (36) cardiovascular agents, such as aspirin (ASA) (enteric coated ASA); (37) i-blocker antianginals, such as **atenolol** and **propranolol**; (38) calcium-channel blocker antianginals, such as nifedipine and verapamil; (39) nitrate antianginals, such as isosorbide dinitrate (ISDN); (40) cardiac glycoside. . . as digoxin; (41) class I antiarrhythmics, such as lidocaine, mexiletine, phenytoin, procainamide, and quinidine; (42) class II antiarrhythmics, such as **atenolol**, **metoprolol**, **propranolol**, and timolol; (43) class III antiarrhythmics, such as amiodarone; (44) class IV antiarrhythmics, such as diltiazem and verapamil; (45) α-blocker. . . such as prazosin; (46) angiotensin-converting enzyme inhibitor (ACE inhibitor) antihypertensives, such as captopril and enalapril; (47) β-blocker antihypertensives, such as **atenolol**, **metoprolol**, nadolol, and propanolol; (48) calcium-channel blocker antihypertensive agents, such as diltiazem and nifedipine; (49) central-acting adrenergic antihypertensives, such as clonidine. . . such as gemfibrozil and probucol; (53) bile acid sequestrant antilipemics, such as cholestyramine; (54) HMG-CoA reductase inhibitor antilipemics, such as **lovastatin** and pravastatin; (55) inotropes, such as amrinone, dobutamine, and dopamine; (56) cardiac glycoside inotropes, such as digoxin; (57) thrombolytic agents,. . .

L8 ANSWER 13 OF 96 USPATFULL

Full-text

ACCESSION NUMBER: 2000:160610 USPATFULL

TITLE: Biodegradable terephthalate polyester-poly (phosphonate) compositions, articles, and methods of using the same

INVENTOR(S): Mao, Hai-quan, Towson, MD, United States
Leong, Kam W., Ellicott City, MD, United States
Zhao, Zhong, Ellicott City, MD, United States
Dang, Wenbin, Ellicott City, MD, United States
English, James P., Chelsea, AL, United States
Nowotnik, David P., Kingsville, MD, United States

PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., Baltimore, MD, United States (U.S. corporation)
Johns Hopkins University School of Medicine, Baltimore, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6153212		20001128	
APPLICATION INFO.:	US 1998-165375		19981002	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Azpuru, Carlos A.
LEGAL REPRESENTATIVE: Howrey Simon Arnold & White, LLP
NUMBER OF CLAIMS: 59
EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 1448
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A medical device is described comprising a biodegradable terephthalate copolymer comprising the recurring monomeric units shown in formula I below: ##STR1## wherein R is a divalent organic moiety; R' is an aliphatic, aromatic, or heterocyclic residue; x is ≥1; and n is 3-7,500, and where the biodegradable terephthalate copolymer is sufficiently pure to be biocompatible and is capable of forming biocompatible residues upon biodegradation. In addition, compositions containing the copolymers and biologically active substances, articles useful for implantation or injection into the body fabricated from the compositions, and methods for controllably releasing biologically active substances using the copolymers, are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . as pilocarpine; (32) cholinesterase inhibitor parasympathomimetics, such as pyridostigmine; (33) α-blocker sympatholytics, such as prazosin; (34) β-blocker sympatholytics, such as **atenolol**; (35) adrenergic agonist sympathomimetics, such as albuterol and dobutamine; (36) cardiovascular agents, such as aspirin (ASA) (enteric coated ASA); (37) β-blocker antianginals, such as **atenolol** and **propranolol**; (38) calcium-channel blocker anti-anginals, such as nifedipine and verapamil; (39) nitrate antianginals, such as isosorbide dinitrate (ISDN); (40) cardiac glycoside. . . as digoxin; (41) class I antiarrhythmics, such as lidocaine, mexiletine, phenytoin, procainamide, and quinidine; (42) class II antiarrhythmics, such as **atenolol**, **metoprolol**, **propranolol**, and timolol; (43) class III antiarrhythmics, such as amiodarone; (44) class IV antiarrhythmics, such as diltiazem and verapamil; (45) α-blocker. . . such as prazosin; (46) angiotensin-converting enzyme inhibitor (ACE inhibitor) antihypertensives, such as captopril and enalapril; (47) β-blocker antihypertensives, such as **atenolol**, **metoprolol**, nadolol, and propanolol; (48) calcium-channel blocker antihypertensive agents, such as diltiazem and nifedipine; (49) central-acting adrenergic antihyper-tensives, such as clonidine. . . such as gemfibrozil and probucol; (53) bile acid sequestrant anti-lipemics, such as cholestyramine; (54) HMG-COA reductase inhibitor anti-lipemics, such as **lovastatin** and pravastatin; (55) inotropes, such as amrinone, dobutamine, and dopamine; (56) cardiac glycoside inotropes, such as digoxin; (57) thrombolytic agents,. . .

L8 ANSWER 14 OF 96 USPATFULL
Full-text
ACCESSION NUMBER: 1999:170710 USPATFULL
TITLE: Two-stage solution polymerization of high molecular weight poly(phosphoesters)
INVENTOR(S): Zhao, Zhong, Ellicott City, MD, United States
Mao, Hai-quan, Towson, MD, United States
Leong, Kam W., Ellicott City, MD, United States
PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., Baltimore, MD, United States (U.S. corporation)
Johns Hopkins University, Baltimore, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6008318		19991228
APPLICATION INFO.:	US 1998-98620		19980617 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1997-877624, filed on 18 Jun 1997, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Truong, Duc
LEGAL REPRESENTATIVE: Howrey & Simon
NUMBER OF CLAIMS: 38
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 1244
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A process for making a phosphoester polymer comprising the recurring monomeric units of formula I: ##STR1## wherein: X is --O-- or --NR"--, where R" is H or alkyl;

L is a divalent organic moiety;

R' is H, alkyl, alkoxy, aryl, aryloxy, heterocyclic, or heterocycloxy; and

n is between about 25 to 2,000,

is described. The process comprises the steps of:

(a) polymerizing in the presence of a solvent p moles of a di-XH compound having formula II:

H--X--L--X--H II

wherein X and L are as defined above, with q moles, where p≈q, of a phosphorodihalo compound to form a polymer of formula I, wherein n is about 12 to 1000, having a first molecular weight Mw, wherein the solvent is present in an amount greater than about 5 ml of solvent per gram of compound of formula II;

(b) removing at least about 25% of the solvent to form a more concentrated reaction mixture; and

(c) further polymerizing the concentrated reaction mixture for an additional time sufficient to produce a polymer of formula I wherein n is between about 25 and 2,000, the polymer having a second molecular weight Mw, which is significantly higher than Mw.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . as pilocarpine; (32) cholinesterase inhibitor parasympathomimetics, such as pyridostigmine; (33) α-blocker sympatholytics, such as prazosin; (34) β-blocker sympatholytics, such as **atenolol**; (35) adrenergic agonist sympathomimetics, such as albuterol and dobutamine; (36) cardiovascular agents, such as aspirin (ASA) (enteric coated ASA); (37) β-blocker antianginals, such as **atenolol** and **propranolol**; (38) calcium-channel blocker antianginals, such as nifedipine and verapamil; (39) nitrate antianginals, such as isosorbide dinitrate (ISDN); (40) cardiac glycoside. . . as digoxin; (41) class I antiarrhythmics, such as lidocaine, mexiletine, phenytoin, procainamide, and quinidine; (42) class II antiarrhythmics, such as **atenolol**, **metoprolol**, **propranolol**, and timolol; (43) class III antiarrhythmics, such as amiodarone; (44) class IV antiarrhythmics, such as diltiazem and verapamil; (45) α-blocker. . . such as prazosin; (46) angiotensin-converting enzyme inhibitor (ACE inhibitor) antihypertensives, such as captopril and enalapril; (47) β-blocker antihypertensives, such as **atenolol**, **metoprolol**, nadolol, and propanolol; (48) calcium-channel blocker antihypertensive agents, such as diltiazem and nifedipine; (49) central-acting adrenergic antihypertensives, such as clonidine. . . such as gemfibrozil and probucol; (53) bile acid sequestrant antilipemics, such as cholestyramine; (54) HMG-CoA reductase inhibitor antilipemics, such as **lovastatin** and pravastatin; (55) inotropes, such as amrinone, dobutamine, and dopamine; (56) cardiac glycoside inotropes, such as digoxin; (57) thrombolytic agents,. . .

L8 ANSWER 15 OF 96 USPATFULL

Full-text

ACCESSION NUMBER:	1999:110440 USPATFULL
TITLE:	Solution polymerization of high molecular weight poly(phosphoesters) in toluene
INVENTOR(S):	Zhao, Zhong, Towson, MD, United States
PATENT ASSIGNEE(S):	Guilford Pharmaceuticals Inc., Baltimore, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5952451		19990914
APPLICATION INFO.:	US 1998-102813		19980623 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1997-884382, filed on 27 Jun 1997		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Mosley, Terressa		

LEGAL REPRESENTATIVE: Nath & Associates, Nath, Gary M., Drost, Patricia M.
NUMBER OF CLAIMS: 46
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1148
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A process for making a high molecular weight poly(phosphoester) composition comprising:

(i) a biologically active substance; and

(ii) a poly(phosphoester) with the recurring monomeric units: ##STR1## wherein X is --O-- or --NR"--, where R" is H or alkyl; L is a divalent organic moiety, with the proviso that L cannot have the formula ##STR2## R' is H, alkyl, alkoxy, aryl, aryloxy, heterocyclic, or heterocycloxy; and n is from about 25 to 2000,

is described. The process comprises the steps of:

(a) substantially dissolving p moles of a di--XH compound in a solvent comprising more than 75% toluene at a first temperature between about -75° C. and +60° C. to form a reaction mixture;

(b) while maintaining the reaction mixture at the first temperature, adding q moles, where p≈q, of a phosphorodihalo compound;

(c) gradually increasing said first temperature at a rate of less than about 1.5° C. per minute as necessary to achieve a second temperature between about 0° C. and 150° C., and mixing the reaction mixture at the second temperature to form the polymer of formula I; and

(d) isolating the polymer of formula I.

(e) incorporating the biologically active substance into the polymer of formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DRWD . . . as pilocarpine; (32) cholinesterase inhibitor parasympathomimetics, such as pyridostigmine; (33) α-blocker sympatholytics, such as prazosin; (34) β-blocker sympatholytics, such as **atenolol**; (35) adrenergic agonist sympathomimetics, such as albuterol and dobutamine; (36) cardiovascular agents, such as aspirin (ASA) (enteric coated ASA); (37) β-blocker antianginals, such as **atenolol** and **propranolol**; (38) calcium-channel blocker antianginals, such as nifedipine and verapamil; (39) nitrate antianginals, such as isosorbide dinitrate (ISDN); (40) cardiac glycoside. . . as digoxin; (41) class I antiarrhythmics, such as lidocaine, mexiletine, phenytoin, procainamide, and quinidine; (42) class II antiarrhythmics, such as **atenolol**, **metoprolol**, **propranolol**, and timolol; (43) class III antiarrhythmics, such as amiodarone; (44) class IV antiarrhythmics, such as diltiazem and verapamil; (45) α-blocker. . . such as prazosin; (46) angiotensin-converting enzyme inhibitor (ACE inhibitor) antihypertensives, such as captopril and enalapril; (47) 9-blocker antihypertensives, such as **atenolol**, **metoprolol**, nadolol, and propanolol; (48) calcium-channel blocker antihypertensive agents, such as diltiazem and nifedipine; (49) central-acting adrenergic antihypertensives, such as clonidine. . . such as gemfibrozil and probucol; (53) bile acid sequestrant antilipemics, such as cholestyramine; (54) HMG-CoA reductase inhibitor antilipemics, such as **lovastatin** and pravastatin; (55) inotropes, such as amrinone, dobutamine, and dopamine; (56) cardiac glycoside inotropes, such as digoxin; (57) thrombolytic agents,. . .

=> d ibib abs kwic 16-20

L8 ANSWER 16 OF 96 USPATFULL
Full-text
ACCESSION NUMBER: 96:43387 USPATFULL
TITLE: Biodegradable controlled release flash flow melt-spun delivery system
INVENTOR(S): Fuisz, Richard C., Great Falls, VA, United States
PATENT ASSIGNEE(S): Fuisz Technologies Ltd., Chantilly, VA, United States

(U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5518730		19960521	
APPLICATION INFO.:	US 1992-893238		19920603	(7)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Webman, Edward J.			
LEGAL REPRESENTATIVE:	Hoffmann & Baron			
NUMBER OF CLAIMS:	28			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)			
LINE COUNT:	1072			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Biodegradable controlled release delivery systems using melt-spun biodegradable polymers as carriers for bio-effecting agents such as pharmaceutical actives are disclosed. Oral dosage forms as well as implants are described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . allantoin; aloe; aluminum acetate, carbonate, chlorohydrate, hydroxide; alprozolam; amino acids; aminobenzoic acid; amoxicillin; ampicillin; amsacrine; amsalog; anethole; ascorbic acid; aspartame; **atenolol**; bacitracin; balsam peru; BCNU (carmustine) beclomethasone dipropionate; benzocaine; benzoic acid; benzophenones; benzoyl peroxide; bethanechol; biotin; bisacodyl; bornyl acetate; bromopheniramine maleate;. . . insulin; iodine; ipecac; iron; isoxicam; ketamine; koalin; lactic acid; lanolin; lecithin; leuprolide acetate; lidocaine and its hydrochloride salt; lifinopril; liotrix; **lovastatin**; luteinizing hormone; LHRH (luteinizing hormone releasing hormone); magnesium carbonate, hydroxide, salicylate, trisilocate; mefenamic acid; meclofenanic acid; meclofenamate sodium; medroxyprogesterone acetate; methenamine mandelate; menthol; meperidine hydrochloride; metaproterenol sulfate; methyl nicotinate; methyl salicylate; methylcellulose; methsuximide; metronidazole and its hydrochloride; **metoprolol** tartrate; miconazole nitrate; mineral oil; minoxidil; morphine; naproxen and its sodium salt; nifedipine; neomycin sulfate; niacin; niacinamide; nicotine; nicotinamide; nitroglycerin;. . .

CLM What is claimed is:

. . . aloe, aluminum acetate, aluminum carbonate, aluminum chlorohydrate, aluminum hydroxide, alprozolam, amino acids, aminobenzoic acid, amoxicillin, ampicillin, amsacrine, amsalog, anethole, aspartame, **atenolol**, bacitracin, balsam peru, beclomethasone dipropionate, benzocaine, benzoic acid, benzophenones, benzoyl peroxide, biotin, bisacodyl, bornyl acetate, bromopheniramine maleate, buspirone, caffeine, calamine,. . . sulfate, ibuprofen, indomethacin, inositol, insulin, iodine, ipecac, iron, isoxicam, ketamine, koalin, lactic acid, lanolin, lecithin, lidocaine, lidocaine hydrochloride, lifinopril, liotrix, **lovastatin**, magnesium carbonate, magnesium hydroxide, magnesium salicylate, magnesium trisilocate, mefenamic acid, meclofenanic acid, meclofenamate sodium, medroxyprogesterone acetate, methenamine mandelate, menthol, meperidine hydrochloride, metaproterenol sulfate, methyl nicotinate, methyl salicylate, methylcellulose, methsuximide, metromidazole, metromidazole hydrochloride, **metoprolol** tartrate, miconazole nitrate, mineral oil, minoxidil, morphine, naproxen, naproxen sodium, nifedipine, neomycin sulfate, niacin, niacinamide, nicotine, nicotinamide, nitroglycerin, nonoxynol-9, norethindone,. . .

. . . isopropanol, allantoin, aloe, aluminum acetate, aluminum carbonate, chlorohydrate, hydroxide, alprozolam, amino acids, aminobenzoic acid, amoxicillin, ampicillin, amsacrine, amsalog, anethole, aspartame, **atenolol**, bacitracin, balsam peru, beclomethasone dipropionate, benzocaine, benzoic acid, benzophenones, benzoyl peroxide, biotin, bisacodyl, bornyl acetate, bromopheniramine maleate, buspirone, caffeine, calamine,. . . sulfate, ibuprofen, indomethacin, inositol, insulin, iodine, ipecac, iron, isoxicam, ketamine, koalin, lactic acid, lanolin, lecithin, lidocaine, lidocaine hydrochloride, lifinopril, liotrix, **lovastatin**, magnesium carbonate, magnesium hydroxide, salicylate, magnesium trisilocate, mefenamic acid, meclofenanic acid, meclofenamate sodium, medroxyprogesterone acetate, methenamine mandelate, menthol, meperidine hydrochloride, metaproterenol sulfate, methyl nicotinate, methyl salicylate, methylcellulose, methsuximide, metromidazole, metromidazole hydrochloride, **metoprolol** tartrate, miconazole nitrate, mineral oil, minoxidil, morphine, naproxen, naproxen

sodium, nifedipine, neomycin sulfate, niacin, niacinamide, nicotine, nicotinamide, nitroglycerin, nonoxynol-9, norethindone,. . .

L8 ANSWER 17 OF 96 MEDLINE
Full-text
ACCESSION NUMBER: 2000173010 MEDLINE
DOCUMENT NUMBER: 20173010 PubMed ID: 10709776
TITLE: Effects of the antifungal agents on oxidative drug metabolism: clinical relevance.
AUTHOR: Venkatakrishnan K; von Moltke L L; Greenblatt D J
CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, Tufts University School of Medicine, Boston, Massachusetts 02111, USA.
CONTRACT NUMBER: DA-05258 (NIDA)
MH-19924 (NIMH)
MH-34223 (NIMH)
+
SOURCE: CLINICAL PHARMACOKINETICS, (2000 Feb) 38 (2) 111-80. Ref: 539
Journal code: DG5; 7606849. ISSN: 0312-5963.
PUB. COUNTRY: New Zealand
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000413
Last Updated on STN: 20000413
Entered Medline: 20000407

AB This article reviews the metabolic pharmacokinetic drug-drug interactions with the systemic antifungal agents: the azoles ketoconazole, miconazole, itraconazole and fluconazole, the allylamine terbinafine and the sulfonamide sulfamethoxazole. The majority of these interactions are metabolic and are caused by inhibition of cytochrome P450 (CYP)-mediated hepatic and/or small intestinal metabolism of coadministered drugs. Human liver microsomal studies in vitro, clinical case reports and controlled pharmacokinetic interaction studies in patients or healthy volunteers are reviewed. A brief overview of the CYP system and the contrasting effects of the antifungal agents on the different human drug-metabolising CYP isoforms is followed by discussion of the role of P-glycoprotein in presystemic extraction and the modulation of its function by the antifungal agents. Methods used for in vitro drug interaction studies and in vitro-in vivo scaling are then discussed, with specific emphasis on the azole antifungals. Ketoconazole and itraconazole are potent inhibitors of the major drug-metabolising CYP isoform in humans, CYP3A4. Coadministration of these drugs with CYP3A substrates such as cyclosporin, tacrolimus, alprazolam, triazolam, midazolam, nifedipine, felodipine, **simvastatin**, **lovastatin**, vincristine, terfenadine or astemizole can result in clinically significant drug interactions, some of which can be life-threatening. The interactions of ketoconazole with cyclosporin and tacrolimus have been applied for therapeutic purposes to allow a lower dosage and cost of the immunosuppressant and a reduced risk of fungal infections. The potency of fluconazole as a CYP3A4 inhibitor is much lower. Thus, clinical interactions of CYP3A substrates with this azole derivative are of lesser magnitude, and are generally observed only with fluconazole dosages of > or =200 mg/day. Fluconazole, miconazole and sulfamethoxazole are potent inhibitors of CYP2C9. Coadministration of phenytoin, warfarin, sulfamethoxazole and losartan with fluconazole results in clinically significant drug interactions. Fluconazole is a potent inhibitor of CYP2C19 in vitro, although the clinical significance of this has not been investigated. No clinically significant drug interactions have been predicted or documented between the azoles and drugs that are primarily metabolised by CYP1A2, 2D6 or 2E1. Terbinafine is a potent inhibitor of CYP2D6 and may cause clinically significant interactions with coadministered substrates of this isoform, such as nortriptyline, desipramine, perphenazine, **metoprolol**, encainide and propafenone. On the basis of the existing in vitro and in vivo data, drug interactions of terbinafine with substrates of other CYP isoforms are unlikely.

L8 ANSWER 18 OF 96 MEDLINE
Full-text
ACCESSION NUMBER: 96306611 MEDLINE
DOCUMENT NUMBER: 96306611 PubMed ID: 8729584

TITLE: Development and pharmacology of fluvastatin.
AUTHOR: Jokubaitis L A
CORPORATE SOURCE: Cardiovascular Clinical Research, Sandoz Research Institute, East Hanover, NJ 07936, USA.
SOURCE: BRITISH JOURNAL OF CLINICAL PRACTICE. SUPPLEMENT, (1996 Jan) 77A 11-5. Ref: 4
Journal code: AVL; 8007786. ISSN: 0262-8767.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961025
Last Updated on STN: 19980206
Entered Medline: 19961011

AB Fluvastatin is the first synthetic 3-hydroxy-3-methylglutaryl coenzyme A (HMGCoA) reductase inhibitor to be approved for clinical use, and has been studied extensively in humans since 1986. It is structurally distinct from the other currently available HMGCoA reductase inhibitors (**lovastatin**, **simvastatin**, and pravastatin), leading to unique biopharmaceutical properties relative to the other agents of this class. Absorption of fluvastatin is virtually complete across all species, including man, and is not affected by the presence of food. Systemic exposure is limited, as fluvastatin is subject to first-pass metabolism, and the plasma half-life of the drug is approximately 30 minutes. Some 95% of a single dosage of fluvastatin is excreted via the biliary route, with less than 2% of this being the parent compound. Additionally, there is no evidence of circulating active metabolites or accumulation during chronic dosing. Studies of the effect of food on the pharmacokinetics of fluvastatin have demonstrated marked reductions in the rate of bioavailability--from 40% to 60%; however, a comparison of fluvastatin administration with the evening meal or at bedtime has revealed no significant differences in the extent of bioavailability (area under the curve) of these two regimens. Furthermore, no significant difference in pharmacodynamic effect (reduction in low-density lipoprotein cholesterol levels) could be ascertained between mealtime dosing and bedtime dosing. The pharmacokinetics of fluvastatin have also been assessed in various demographic groups. Relative to the general population, plasma concentrations of fluvastatin do not vary as a function of either age or gender. In addition, administration to a patient population with hepatic insufficiency resulted in a 2.5-fold increase in both the rate and extent of bioavailability relative to controls. Also, although minimal alterations of fluvastatin clearance in patients with renal insufficiency are anticipated due to limited renal excretion (5%), a study in this patient group is currently underway to examine this further. Interaction studies have been performed with fluvastatin and several drugs with which it might be coadministered. Cholestyramine, an anionic-binding resin, has a considerable effect in lowering the rate and extent of fluvastatin bioavailability. Although this effect was noted even when cholestyramine was given 4 hours prior to fluvastatin, this regimen did not result in diminished efficacy. Further, no effects on either warfarin levels or prothrombin times were observed in a study involving concomitant administration of warfarin and fluvastatin. Moreover, additional interaction studies with niacin and **propranolol** have not demonstrated any effect on fluvastatin plasma levels, and administration to a patient population chronically receiving digoxin resulted in no difference in the extent of bioavailability of digoxin relative to control data. The results generated to date in clinical pharmacokinetic studies with fluvastatin thus support its use in a broad population of hypercholesterolaemic patients.

L8 ANSWER 19 OF 96 BIOSIS COPYRIGHT 2001 BIOSIS
Full-text
ACCESSION NUMBER: 1992:436123 BIOSIS
DOCUMENT NUMBER: BA94:88248
TITLE: PRIMARY AND SECONDARY PREVENTION OF CORONARY ARTERY DISEASE.
AUTHOR(S): GOTTO A M JR
CORPORATE SOURCE: DEP. MED., MS SM-1423, BAYLOR COLL. MED., 6550 FANNIN, HOUSTON, TEXAS 77030.
SOURCE: CURR OPIN CARDIOL, (1992) 7 (4), 553-562.
CODEN: COPCE3.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB A variety of new results from clinical studies point toward improved assessment of and intervention in risk factors for coronary artery disease. Separate analyses of Helsinki Heart Study and Prospective Cardiovascular Muenster (PROCAM) data showed the combination of triglyceride elevation and a high ratio of total cholesterol or low-density lipoprotein cholesterol (LDL-C) to high-density lipoprotein cholesterol (HDL-C) to confer greater risk of coronary artery disease than LDL-C elevation alone. In the Physicians' Health Study (PHS), a change of 1 unit in the total to HDL cholesterol ratio was associated with a 53% change in risk for myocardial infarction after adjustment for other risk factors. Findings from these studies support recommendations by the February 1992 US National Institutes of Health Consensus Development Conference on Triglyceride, High Density Lipoprotein, and Coronary Heart Disease that not only total cholesterol but also HDL-C be measured in healthy individuals to assess coronary artery disease risk and that HDL-C and triglyceride be measured in additional clinical circumstances, eg, in patients with known coronary artery disease or with desirable total cholesterol and two or more risk factors and in such disorders as hypertension and diabetes mellitus, to refine risk assessment. Strong evidence associates much-increased coronary artery disease risk with atherogenic lipoprotein phenotype B, in which presumably atherogenic small, dense LDL particles predominate. A meta-analysis of major cholesterol-lowering trials suggested that targeted secondary intervention could have a major impact on coronary artery disease events in the entire population, because there were 27 fewer myocardial infarctions than expected per 1000 patients treated across eight secondary-intervention trials, compared with six per 1000 across four primary-prevention trials, and because half of all myocardial infarctions occur in men with a history of coronary artery disease. Noteworthy new results have also been published on nonlipid variables in relation to coronary artery disease risk, incldуing aspirin use, **propranolol** use, tissue plasminogen activator antigen level, family history of myocardial infarction, and adipose distribution. There are promising new findings that directing educational programs on lifestyle risk factors toward families or communities can be effective. The approval in 1991 of two additional reductase inhibitors (pravastatin and **simvastatin**) for use in the United States provides options in a class of drugs with excellent efficacy and safety records, recently bolstered by publication of the findings of the Expanded Clinical Evaluation of **Lovastatin** (EXCEL) study.

IT Miscellaneous Descriptors
REVIEW HUMAN **LOVASTATIN** PRAVASTATIN **SIMVASTATIN** ENZYME INHIBITOR-DRUG ASPIRIN **PROPRANOLOL** NITRATE ANTIATHEROGENIC-DRUG TISSUE PLASMINOGEN ACTIVATOR THROMBOLYTIC-DRUG HIGH DENSITY LIPOPROTEIN CHOLESTEROL LOW DENSITY LIPOPROTEIN CHOLESTEROL MYOCARDIAL INFARCTION HYPERTENSION DIABETES MELLITUS

L8 ANSWER 20 OF 96 MEDLINE
Full-text
ACCESSION NUMBER: 2000495716 MEDLINE
DOCUMENT NUMBER: 20398558 PubMed ID: 10940116
TITLE: Infiltrating basal cell carcinoma in the setting of a venous ulcer.
AUTHOR: Lutz M E; Davis M D; Otley C C
CORPORATE SOURCE: Department of Dermatology, Mayo Clinic and Mayo Foundation, Rochester, MN 55905, USA.
SOURCE: INTERNATIONAL JOURNAL OF DERMATOLOGY, (2000 Jul) 39 (7) 519-20.
Journal code: GR2; 0243704. ISSN: 0011-9059.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001018

AB A 77-year-old man was referred with a 5-year history of an intermittently painful, nonhealing right medial ankle ulcer. The ulcer had not responded to multiple treatment modalities, including Unna boots, compression therapy, sclerotherapy, and split-thickness skin grafting. The past medical history was significant for a deep venous thrombosis in the right leg 30 years earlier (treated with warfarin for 3 months) and a history of greater saphenous vein harvesting for coronary bypass grafting 28 years previously. After the vein stripping, the patient had suffered from increasing right leg edema and stasis changes in the right leg. His

history was also remarkable for coronary artery disease, dyslipidemia, and lymphoma treated with chemotherapy 8 years before presentation, with no evidence of recurrence. He had stopped smoking approximately 20 years earlier. Medications included **atenolol**, **simvastatin**, nicardipine, nitroglycerin, and aspirin. Skin examination revealed a 3.0 x 3.5-cm ulcer adjacent to the medial malleolus. The edges of the ulcer appeared raised and rolled (Fig. 1). Centrally, there was granulation tissue, which appeared healthy. There were surrounding dermatitic changes. Dorsalis pedis and the posterior tibial pulses were normal. Noninvasive vascular studies revealed severe venous incompetence of the right popliteal and superficial veins. Arterial studies and transcutaneous oximetry were normal. Computed tomographic scan of the pelvis did not reveal any adenopathy, and radiographic imaging did not reveal any bony changes suggestive of osteomyelitis. Biopsy of the ulcer edge and base showed infiltrating basal cell carcinoma (Fig. 2). Mohs' micrographic surgery required three layers; the final extent of the ulcer was 7.8 x 6.9 cm. A split-thickness skin graft was placed.

=> d ti tot

L8 ANSWER 1 OF 96 MEDLINE
TI Pharmacokinetic interaction between **propranolol** and the HMG-CoA reductase inhibitors pravastatin and **lovastatin**.

L8 ANSWER 2 OF 96 MEDLINE
TI Simvastatin inhibits noradrenaline-induced hypertrophy of cultured neonatal rat cardiomyocytes.

L8 ANSWER 3 OF 96 MEDLINE
TI [Severe rhabdomyolysis in a patient receiving lovastatin, danazol, and doxycycline].
Rhabdomyolyse severe chez un patient recevant lovastatine, danazol et doxycycline.

L8 ANSWER 4 OF 96 USPATFULL
TI In vivo delivery methods and compositions

L8 ANSWER 5 OF 96 MEDLINE
TI Clinical implications of the biopharmaceutical properties of fluvastatin.

L8 ANSWER 6 OF 96 CAPLUS COPYRIGHT 2001 ACS
TI Formulation for the prevention of cardiovascular disease

L8 ANSWER 7 OF 96 USPATFULL
TI Biodegradable polymers chain-extended by phosphates, compositions, articles and methods for making and using the same

L8 ANSWER 8 OF 96 MEDLINE
TI Nightmares and sleep disturbances with **simvastatin** and **metoprolol**.

L8 ANSWER 9 OF 96 MEDLINE
TI In the past 12 to 18 months, my level of anxiety has increased significantly. I have been on **atenolol** and **simvastatin** (Zocor) for the past couple of years. Is there anything in these drugs that could cause this anxiety?.

L8 ANSWER 10 OF 96 BIOSIS COPYRIGHT 2001 BIOSIS
TI Nightmares and sleep disturbances with **simvastatin** and **metoprolol**.

L8 ANSWER 11 OF 96 BIOSIS COPYRIGHT 2001 BIOSIS
TI Effects of hypolipemic therapy on the pharmacokinetics of propranolol.

L8 ANSWER 12 OF 96 USPATFULL
TI Biodegradable terephthalate polyester-poly (phosphate) polymers, compositions, articles, and methods for making and using the same

L8 ANSWER 13 OF 96 USPATFULL
TI Biodegradable terephthalate polyester-poly (phosphonate) compositions, articles, and methods of using the same

L8 ANSWER 14 OF 96 USPATFULL
TI Two-stage solution polymerization of high molecular weight poly(phosphoesters)

L8 ANSWER 15 OF 96 USPATFULL

TI Solution polymerization of high molecular weight poly(phosphoesters) in toluene

L8 ANSWER 16 OF 96 USPATFULL
TI Biodegradable controlled release flash flow melt-spun delivery system

L8 ANSWER 17 OF 96 MEDLINE
TI Effects of the antifungal agents on oxidative drug metabolism: clinical relevance.

L8 ANSWER 18 OF 96 MEDLINE
TI Development and pharmacology of fluvastatin.

L8 ANSWER 19 OF 96 BIOSIS COPYRIGHT 2001 BIOSIS
TI PRIMARY AND SECONDARY PREVENTION OF CORONARY ARTERY DISEASE.

L8 ANSWER 20 OF 96 MEDLINE
TI Infiltrating basal cell carcinoma in the setting of a venous ulcer.

L8 ANSWER 21 OF 96 MEDLINE
TI Failure of educational videotapes to improve medication compliance in a health maintenance organization.

L8 ANSWER 22 OF 96 MEDLINE
TI Cataracts in systemic diseases and syndromes.

L8 ANSWER 23 OF 96 MEDLINE
TI Secondary prevention for ischemic heart disease. Relative numbers needed to treat with different therapies.

L8 ANSWER 24 OF 96 USPATFULL
TI Clear oil-containing pharmaceutical compositions

L8 ANSWER 25 OF 96 USPATFULL
TI Bioadhesive progressive hydration tablets and methods of making and using the same

L8 ANSWER 26 OF 96 USPATFULL
TI Method for preventing or reducing photosensitivity and or photoxicity reaction to medications

L8 ANSWER 27 OF 96 USPATFULL
TI Stereospecific delivery of a drug using electrotransport

L8 ANSWER 28 OF 96 USPATFULL
TI Medicinal and/or nutritional microcapsules for oral administration

L8 ANSWER 29 OF 96 USPATFULL
TI Method for preventing or reducing photosensitivity and/or phototoxicity reactions to medications

L8 ANSWER 30 OF 96 MEDLINE
TI Care of adults with type 2 diabetes mellitus. A review of the evidence.

L8 ANSWER 31 OF 96 USPATFULL
TI Solid dosage form with polymeric binder

L8 ANSWER 32 OF 96 USPATFULL
TI TREATING OR PREVENTING THE EARLY STAGES OF DEGENERATION OF ARTICULAR CARTILAGE OR SUBCHONDRAL BONE IN MAMMALS USING CARPROFEN AND DERIVATIVES

L8 ANSWER 33 OF 96 USPATFULL
TI Process for producing solid dosage forms by extrusion

L8 ANSWER 34 OF 96 USPATFULL
TI Solid medicaments obtained by extrusion of an isomalt-containing polymer-active substance melt

L8 ANSWER 35 OF 96 USPATFULL
TI Solid foamed active substance preparations

L8 ANSWER 36 OF 96 USPATFULL
TI Production of lenticular tablets by melt calendering

L8 ANSWER 37 OF 96 USPATFULL

TI Method of producing multi-layer medicaments in solid form for oral or rectal administration

L8 ANSWER 38 OF 96 USPATFULL
TI Production of solid drug forms

L8 ANSWER 39 OF 96 USPATFULL
TI Process and apparatus for the production of divisible tablets

L8 ANSWER 40 OF 96 USPATFULL
TI Process for producing solid drug forms having at least two phases

L8 ANSWER 41 OF 96 USPATFULL
TI Solid active extrusion compound preparations containing low-substituted hydroxypropylcellulose

L8 ANSWER 42 OF 96 USPATFULL
TI Production of covered tablets

L8 ANSWER 43 OF 96 USPATFULL
TI Controlled release simvastatin delivery device

L8 ANSWER 44 OF 96 USPATFULL
TI Controlled release drug suspension delivery device

L8 ANSWER 45 OF 96 USPATFULL
TI Controlled release nifedipine delivery device

L8 ANSWER 46 OF 96 USPATFULL
TI Controlled release drug dispersion delivery device

L8 ANSWER 47 OF 96 USPATFULL
TI Spheronization process using charged resins

L8 ANSWER 48 OF 96 USPATFULL
TI Process for producing a tablet core aperture

L8 ANSWER 49 OF 96 USPATFULL
TI Dosage form for delivering a drug at two different rates

L8 ANSWER 50 OF 96 MEDLINE
TI The impact of specialists on prescribing by general practitioners.

L8 ANSWER 51 OF 96 MEDLINE
TI [An overview of hypertension studies with calcium antagonists]. Oversikt over hypertensjonsstudier med kalsiumantagonister. ASCOT. Anglo-Scandinavian Cardiac Outcomes Trial.

L8 ANSWER 52 OF 96 CAPLUS COPYRIGHT 2001 ACS
TI A case with renovascular hypertension

L8 ANSWER 53 OF 96 BIOSIS COPYRIGHT 2001 BIOSIS
TI Rationale, design, methods and baseline demography of participants of the Anglo-Scandinavian cardiac outcomes trial.

L8 ANSWER 54 OF 96 USPATFULL
TI New compounds, their preparation and use

L8 ANSWER 55 OF 96 USPATFULL
TI Bioadhesive solid dosage form

L8 ANSWER 56 OF 96 USPATFULL
TI Conjugates of dithiocarbamate disulfides with pharmacologically active agents and uses therefor

L8 ANSWER 57 OF 96 USPATFULL
TI Anti-first-pass effect compounds

L8 ANSWER 58 OF 96 USPATFULL
TI Fatty acid-pharmaceutical agent conjugates

L8 ANSWER 59 OF 96 USPATFULL
TI Pharmaceutical compositions in semisolid form and a device for administration thereof

L8 ANSWER 60 OF 96 USPATFULL
TI Spill resistant pharmaceutical compositions in semi-solid form

L8 ANSWER 61 OF 96 USPATFULL
TI Purified galactomannan as an improved pharmaceutical excipient

L8 ANSWER 62 OF 96 USPATFULL
TI Conjugates of dithiocarbamates with pharmacologically active agents and uses therefore

L8 ANSWER 63 OF 96 USPATFULL
TI Medicinal adjuvants consisting of N-subsitituted-o-toluidine derivatives, and percutaneously absorbable preparations comprising the adjuvants

L8 ANSWER 64 OF 96 USPATFULL
TI Pharmaceutical compositions in semisolid form and a device for administration thereof

L8 ANSWER 65 OF 96 USPATFULL
TI Transdermal delivery of medications using a combination of penetration enhancers

L8 ANSWER 66 OF 96 USPATFULL
TI DHA-pharmaceutical agent conjugates of taxanes

L8 ANSWER 67 OF 96 USPATFULL
TI Method of detecting cytopenia that is mediated by drug-dependent antibody binding to blood cells

L8 ANSWER 68 OF 96 USPATFULL
TI Composition and method for treating diabetes

L8 ANSWER 69 OF 96 USPATFULL
TI Method of using deuterated calcium channel blockers

L8 ANSWER 70 OF 96 USPATFULL
TI Methods and compositions for the rapid and enduring relief of inadequate myocardial function

L8 ANSWER 71 OF 96 USPATFULL
TI Use of nebivolol as an anti-atherogenic

L8 ANSWER 72 OF 96 USPATFULL
TI Use of Nebivolol as an anti-atherogenic

L8 ANSWER 73 OF 96 USPATFULL
TI Methods and compositions for the rapid and enduring relief of inadequate myocardial function

L8 ANSWER 74 OF 96 USPATFULL
TI Enhancement of the efficacy of nifedipine by deuteration

L8 ANSWER 75 OF 96 USPATFULL
TI Once daily pharmaceutical tablet having a unitary core

L8 ANSWER 76 OF 96 USPATFULL
TI Method for controlling and/or lowering serum glucose and fatty acid concentrations and hypertensive blood pressure in non-insulin-dependent diabetic patients

L8 ANSWER 77 OF 96 USPATFULL
TI Diffusion-osmotic controlled drug-release pharmaceutical composition and process for preparing same

L8 ANSWER 78 OF 96 USPATFULL
TI Uncoated tablets and method of producing the same

L8 ANSWER 79 OF 96 BIOSIS COPYRIGHT 2001 BIOSIS
TI LONG-TERM TREATMENT FOLLOWING ACUTE MYOCARDIAL INFARCTION.

L8 ANSWER 80 OF 96 USPATFULL
TI Arrays of nucleic acid probes for analyzing biotransformation genes and methods of using the same

L8 ANSWER 81 OF 96 USPATFULL
TI Sachet formulations

L8 ANSWER 82 OF 96 USPATFULL
TI Embedding and encapsulation of controlled release particles

L8 ANSWER 83 OF 96 USPATFULL
TI Dosage forms containing taste masked active agents

L8 ANSWER 84 OF 96 USPATFULL
TI Fatty ester combinations

L8 ANSWER 85 OF 96 USPATFULL
TI Method for treating respiratory distress by sublingual administration of DNA

L8 ANSWER 86 OF 96 USPATFULL
TI Method for treating mucositis by sublingual administration of DNA

L8 ANSWER 87 OF 96 USPATFULL
TI Disintegratable microspheres

L8 ANSWER 88 OF 96 USPATFULL
TI Fast-dissolving comestible units formed under high-speed/high-pressure conditions

L8 ANSWER 89 OF 96 USPATFULL
TI Immediate release dosage forms containing microspheres

L8 ANSWER 90 OF 96 USPATFULL
TI Self-binding shearform compositions

L8 ANSWER 91 OF 96 USPATFULL
TI Method of treating colonic adenomas

L8 ANSWER 92 OF 96 USPATFULL
TI Treatment of otitis media by sublingual administration of DNA

L8 ANSWER 93 OF 96 USPATFULL
TI Fast-dissolving comestible units formed under high-speed/high-pressure conditions

L8 ANSWER 94 OF 96 USPATFULL
TI Self-binding shearform compositions

L8 ANSWER 95 OF 96 USPATFULL
TI Antibiotic oil suspensions

L8 ANSWER 96 OF 96 USPATFULL
TI Nasally administrable compositions

=> d ibib abs kwic 21-23

L8 ANSWER 21 OF 96 MEDLINE
Full-text
ACCESSION NUMBER: 96119408 MEDLINE
DOCUMENT NUMBER: 96119408 PubMed ID: 8564589
TITLE: Failure of educational videotapes to improve medication compliance in a health maintenance organization.
AUTHOR: Powell K M; Edgren B
CORPORATE SOURCE: Diversified Pharmaceutical Services, Minneapolis, MN 55440-9422, USA.
SOURCE: AMERICAN JOURNAL OF HEALTH-SYSTEM PHARMACY, (1995 Oct 15) 52 (20) 2196-9.
Journal code: CBH; 9503023. ISSN: 1079-2082.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960315
Last Updated on STN: 19960315

Entered Medline: 19960306

AB The value of mailed educational videotapes as a means of enhancing compliance with drug therapy was studied. Members of a health maintenance organization with a pharmacy claim for benazepril, **metoprolol**, **simvastatin**, or transdermal estrogen were randomly assigned to a study group or a control group. Subjects in the study group were mailed one of four videotape programs giving information on the drug prescribed and the inferred disease state. Control subjects received no educational materials. Subjects were enrolled from July 1, 1993, through January 2, 1994. Refill data were collected from July 1, 1993, through April 1, 1994. The medication possession ratio (MPR) was calculated as the total number of days' supply of a drug obtained by a member divided by the number of days between the time of enrollment and April 1, 1994, or the date the member was terminated from the plan. A subject was deemed compliant if his or her MPR was > or = 0.80. There were no significant differences in mean MPRs between the study group (n = 1993) and the control group (n = 2253). None of the mean MPRs was > or = 0.80, although 44% of control subjects and 46% of study-group subjects were compliant. Of 97 respondents to a survey mailed to a randomly selected subset of the study group, almost 87% reported that they had viewed the videotapes, and of these subjects, about 88% said they found them very useful or somewhat useful. A one-time mailing of videotapes to patients, with no individual follow-up, did not increase compliance with the medications monitored.

L8 ANSWER 22 OF 96 MEDLINE
Full-text
ACCESSION NUMBER: 95399905 MEDLINE
DOCUMENT NUMBER: 95399905 PubMed ID: 10150840
TITLE: Cataracts in systemic diseases and syndromes.
AUTHOR: Bariciak M D; Nichols B D
CORPORATE SOURCE: University of Western Ontario, London, Canada.
SOURCE: CURRENT OPINION IN OPHTHALMOLOGY, (1995 Feb) 6 (1) 3-8.
Ref: 32
Journal code: BB4; 9011108. ISSN: 1040-8738.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: T
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 20010223
Last Updated on STN: 20010223
Entered Medline: 19951013

AB A comprehensive review of the ophthalmic literature on cataracts during the past year is presented. Topics covered include new epidemiologic associations, diabetic cataracts, and syndromes involving cataracts. Data from the Beaver Dam Eye Study suggest the presence of a recessive gene for nuclear sclerosis. Estrogen exposure may decrease the risk of nuclear sclerosis. The effects of amiodarone, **propranolol**, and **lovastatin** on the lens are discussed. Electron microscopy studies have furthered our understanding of diabetic cataracts and the rare Christmas tree cataract. Two new studies support the adverse effect of extracapsular cataract extraction on diabetic retinopathy. New associations between neurofibromatosis 2 and the lens will aid in the diagnosis of this condition. Other ocular and systemic syndromes are discussed.

AB . . . of a recessive gene for nuclear sclerosis. Estrogen exposure may decrease the risk of nuclear sclerosis. The effects of amiodarone, **propranolol**, and **lovastatin** on the lens are discussed. Electron microscopy studies have furthered our understanding of diabetic cataracts and the rare Christmas tree. . .

L8 ANSWER 23 OF 96 MEDLINE
Full-text
ACCESSION NUMBER: 1998022096 MEDLINE
DOCUMENT NUMBER: 98022096 PubMed ID: 9382659
TITLE: Secondary prevention for ischemic heart disease. Relative numbers needed to treat with different therapies.
AUTHOR: Miller D B
CORPORATE SOURCE: Department of Medicine, University of Western Ontario, London.. dmiller@ampsc.com
SOURCE: ARCHIVES OF INTERNAL MEDICINE, (1997 Oct 13) 157 (18) 2045-52. Ref: 38
Journal code: 7FS; 0372440. ISSN: 0003-9926.
PUB. COUNTRY: United States

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                    Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
                    (REVIEW, TUTORIAL)
LANGUAGE:           English
FILE SEGMENT:       Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:        199711
ENTRY DATE:         Entered STN: 19971224
                    Last Updated on STN: 19971224
                    Entered Medline: 19971110
AB   Secondary prevention of ischemic heart disease refers to the process of
     preventing further morbidity and reducing mortality rates in patients with
     clinical manifestations of the disease. Twenty-five large randomized,
     clinical trials addressing mortality rates and cardiovascular morbidity in
     patients with established ischemic heart disease are reviewed. Broadly
     defined, these were trials of aspirin and antiplatelet agents,
     anticoagulants, beta-blockers, calcium channel blockers,
     angiotensin-converting enzyme inhibitors, lowering of cholesterol levels,
     exercise rehabilitation, and diet or vitamins. In trials using warfarin
     sodium, timolol maleate, propranolol hydrochloride, captopril, ramipril,
     and simvastatin and 2 diet studies, statistically significant
     improvements in total mortality rates were seen. Most other studies showed
     non-significant reductions in total mortality rates, with statistically
     significant reductions in 1 or more measures of cardiovascular morbidity.
     The methods necessary for the reader to calculate the number (of patients)
     needed to treat for other studies are also reviewed. The uses and
     limitations of the number needed to treat as a method to compare studies
     of different interventions in similar populations are discussed.
AB   . . . angiotensin-converting enzyme inhibitors, lowering of cholesterol
     levels, exercise rehabilitation, and diet or vitamins. In trials using
     warfarin sodium, timolol maleate, propranolol hydrochloride, captopril,
     ramipril, and simvastatin and 2 diet studies, statistically significant
     improvements in total mortality rates were seen. Most other studies showed
     non-significant reductions in. . .


=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    70.84     109.00

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -0.59      -0.59

INDEX 'ADISALERTS, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI,
       BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,
       CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB,
       DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...'
ENTERED AT 10:40:50 ON 04 DEC 2001

59 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s lovastatin or simvastatin or atorvastatin or cerivastatin
       3561   FILE ADISALERTS
         37   FILE ADISINSIGHT
        695*  FILE ADISNEWS
         76   FILE AGRICOLA
         44   FILE ANABSTR
          2   FILE AQUASCI
        254   FILE BIOBUSINESS
         11   FILE BIOCOMMERCE
       4318   FILE BIOSIS
         64   FILE BIOTECHABS
         64   FILE BIOTECHDS
        619   FILE BIOTECHNO
        195   FILE CABA
        517   FILE CANCERLIT
       2720   FILE CAPLUS
         26   FILE CEABA-VTB
         16   FILE CEN
        237   FILE CIN
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      268   FILE CONFSCI
  20 FILES SEARCHED...
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       75   FILE DGENE
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       12   FILE FSTA
       22   FILE GENBANK
        7   FILE HEALSAFE
      155   FILE IFIPAT
      283   FILE JICST-EPLUS
        4   FILE KOSMET
      269   FILE LIFESCI
     4116   FILE MEDLINE
        6   FILE NTIS
  47 FILES SEARCHED...
     1874   FILE PASCAL
       34   FILE PHAR
       19   FILE PHIC
     1137   FILE PHIN
     1285   FILE PROMT
     4667   FILE SCISEARCH
        4   FILE SYNTHLINE
     1666   FILE TOXLIT
     1091   FILE USPATFULL
      285   FILE WPIDS
      285   FILE WPINDEX

  51 FILES HAVE ONE OR MORE ANSWERS,   59 FILES SEARCHED IN STNINDEX

L9   QUE LOVASTATIN OR SIMVASTATIN OR ATORVASTATIN OR CERIVASTATIN

=> s propranolol or atenolol or metoprolol
     5752   FILE ADISALERTS
      124   FILE ADISINSIGHT
     1237*  FILE ADISNEWS
      214   FILE AGRICOLA
      848   FILE ANABSTR
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      669   FILE BIOBUSINESS
        5   FILE BIOCOMMERCE
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       42   FILE BIOTECHDS
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    32980   FILE DDFU
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    23131   FILE DRUGB
     1338   FILE DRUGLAUNCH
     2645   FILE DRUGMONOG2
       22   FILE DRUGNL
    34352   FILE DRUGU
       70   FILE DRUGUPDATES
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    76316   FILE EMBASE
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         1   FILE GENBANK
        53   FILE HEALSAFE
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      2802   FILE LIFESCI
     41706   FILE MEDLINE
       234   FILE NIOSHTIC
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         4   FILE PHIC
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       924   FILE PROMT
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       476   FILE WPIDS
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  56 FILES HAVE ONE OR MORE ANSWERS,   59 FILES SEARCHED IN STNINDEX

L10  QUE PROPRANOLOL OR ATENOLOL OR METOPROLOL

=> s l9 and l10
        74   FILE ADISALERTS
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        32*  FILE ADISNEWS
         2   FILE ANABSTR
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         1   FILE CEN
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       268   FILE EMBASE
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         8   FILE IFIPAT
         1   FILE JICST-EPLUS
         1   FILE LIFESCI
  44 FILES SEARCHED...
        19   FILE MEDLINE
         6   FILE PASCAL
        51   FILE PHIN
        31   FILE PROMT
        19   FILE SCISEARCH
         8   FILE TOXLIT
  56 FILES SEARCHED...
       129   FILE USPATFULL
        14   FILE WPIDS
        14   FILE WPINDEX

  29 FILES HAVE ONE OR MORE ANSWERS,   59 FILES SEARCHED IN STNINDEX

L11  QUE L9 AND L10

=> d rank
F1          268   EMBASE
F2          223   DRUGU
F3          204   DDFU
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F4          129   USPATFULL
F5           74   ADISALERTS
F6           51   PHIN
F7           48   CAPLUS
F8           32*  ADISNEWS
F9           31   PROMT
F10          19   MEDLINE
F11          19   SCISEARCH
F12          18   BIOTECHNO
F13          14   BIOSIS
F14          14   WPIDS
F15          14   WPINDEX
F16           8   IFIPAT
F17           8   TOXLIT
F18           6   PASCAL
F19           4   ESBIOBASE
F20           3   EMBAL
F21           2   ADISINSIGHT
F22           2   ANABSTR
F23           2   CANCERLIT
F24           1   BIOBUSINESS
F25           1   CEN
F26           1   DRUGNL
F27           1   DRUGUPDATES
F28           1   JICST-EPLUS
F29           1   LIFESCI


=> fil f1-3 f5 f8-11 f14-15
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     9.18     118.18

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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=> s l11
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L12         680 L11

=> dup rem l12
DUPLICATE IS NOT AVAILABLE IN 'ADISNEWS'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING IS APPROXIMATELY  97% COMPLETE FOR L12
PROCESSING COMPLETED FOR L12
L13          592 DUP REM L12 (88 DUPLICATES REMOVED)
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=> s cardio? and l13
L14         192 CARDIO? AND L13

=> focus
PROCESSING COMPLETED FOR L14
L15         192 FOCUS L14 1-

=> d ibib abs kwic 1-5

L15  ANSWER 1 OF 192  PROMT  COPYRIGHT 2001 Gale Group
Full-text

ACCESSION NUMBER:   1998:588061  PROMT
TITLE:              Follow-Up Data From Landmark Cholesterol Study Indicate
                    Life-Saving Benefits of Zocor(R) Are Maintained.
SOURCE:             PR Newswire, (11 Nov 1998) pp. 0631.
LANGUAGE:           English
WORD COUNT:           8273
                    *FULL TEXT IS AVAILABLE IN THE ALL FORMAT*
AB     DALLAS, Nov. 11 /PRNewswire/ -- Follow-up data from the landmark
     Scandinavian Simvastatin Survival Study (4S) with the Merck & Co., Inc.
     (NYSE: MRK), cholesterol-lowering drug Zocor(R) (simvastatin) have shown
     that the 30 percent reduction in risk of death observed in the original
     5-year study has been maintained during extended 2-year follow-up study,
     with survival benefits now being reported for a median 7.4 years, and in
     some patients for up to 8 years. The data were presented at the 71st
     Scientific Sessions of the American Heart Association (AHA).
       "An important measure of the long-term efficacy and safety profile of a
     cholesterol-lowering medicine is its impact on mortality," said Terje
     Pedersen, M.D., professor of clinical cardiology at Aker University
     Hospital in Oslo, Norway, and principal investigator for 4S. "These
     follow-up data are exciting because they indicate that the life-saving
     benefits of long-term therapy with Zocor seen at the end of the original
     5.4-year trial in patients with high cholesterol and coronary heart
     disease were maintained for an additional two years following the study
     conclusion."
       Recommended Use of Zocor
       In patients with coronary heart disease (CHD) and high cholesterol,
     Zocor is indicated to reduce the risk of total mortality, non-fatal
     myocardial infarction, myocardial revascularization procedures, and stroke
     or transient ischemic attack.  Zocor should be used in addition to diet to
     lower elevated cholesterol levels after diet alone has failed to achieve
     target levels.  In patients who have been hospitalized with an acute
     coronary event, such as a heart attack or worsening chest pain,
     consideration can be given to initiating drug therapy at the time of
     discharge if LDL cholesterol levels are at 130 mg/dL or higher.
      THIS IS AN EXCERPT: COPYRIGHT 1998 PR Newswire Association, Inc.
       DALLAS, Nov. 11 /PRNewswire/ -- Follow-up data from the landmark
     Scandinavian Simvastatin Survival Study (4S) with the Merck & Co., Inc.
     (NYSE: MRK), cholesterol-lowering drug Zocor(R) (simvastatin) have shown
     that the 30 percent reduction in risk of death observed in the original
     5-year study has been maintained.  .  .
       "An  .  .  .  efficacy and safety profile of a cholesterol-lowering
     medicine is its impact on mortality," said Terje Pedersen, M.D., professor
     of clinical cardiology at Aker University Hospital in Oslo, Norway, and
     principal investigator for 4S.  "These follow-up data are exciting because
     they indicate.  .  .
TX     DALLAS, Nov. 11 /PRNewswire/ -- Follow-up data from the landmark
     Scandinavian Simvastatin Survival Study (4S) with the Merck & Co., Inc.
     (NYSE: MRK), cholesterol-lowering drug Zocor(R) (simvastatin) have shown
     that the 30 percent reduction in risk of death observed in the original
     5-year study has been maintained.  .  .
       "An  .  .  .  efficacy and safety profile of a cholesterol-lowering
     medicine is its impact on mortality," said Terje Pedersen, M.D., professor
     of clinical cardiology at Aker University Hospital in Oslo, Norway, and
     principal investigator for 4S.  "These follow-up data are exciting because
     they indicate.  .  .
       Deaths from both cardiovascular and non-cardiovascular causes were
     examined in the analysis of health records.  Of the patients who had been
     treated with Zocor, approximately 2.3.  .  .
       For other cardiovascular and non-cardiovascular deaths, the numbers
     were similar for the two groups.
       Of  .  .  .  The response rate to the survey was 88.4 percent for the
     original placebo group and 89.4 percent for the original simvastatin
```

group. 4S: Driving Treatment Evolution

"The . . . disease," said Sidney C. Smith, Jr., M.D., former president of the AHA and professor and chief of the division of **cardiology** at the University of North Carolina at Chapel Hill. "Many people have benefited throughout the world because of what physicians. . .

(SIMVASTATIN)

ZOCOR* (**simvastatin**) is a lipid-lowering agent that is derived synthetically from a fermentation product of Aspergillus terreus. After oral ingestion, **simvastatin**, which is an inactive lactone, is hydrolyzed to the corresponding beta-hydroxyacid form. This is an inhibitor of 3-hydroxy-3- methylglutaryl-coenzyme A. . .

Simvastatin is butanoic acid,2,2-dimethyl-,1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)-ethyl]-1-naphthalenyl ester, [1S-[1alpha,3alpha,7beta,8beta (2S*,4S*),-8 alpha beta]]. The empirical formula of **simvastatin** is C25H38O5 and its molecular weight is 418.57. Its structural formula is:

Simvastatin is a white to off-white, nonhygroscopic, crystalline powder that is practically insoluble in water, and freely soluble in chloroform, methanol. . .

Tablets ZOCOR for oral administration contain either 5 mg, 10 mg, 20 mg, 40 mg or 80 mg of **simvastatin** and the following inactive ingredients: cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, iron oxides, lactose, magnesium stearate, starch, talc, titanium dioxide and. . .

The . . . for coronary heart disease (CHD). The independent effect of raising HDL-C or lowering TG on the risk of coronary and **cardiovascular** morbidity and mortality has not been determined.

In the Scandinavian **Simvastatin** Survival Study (4S), the effect of improving lipoprotein levels with ZOCOR on total mortality was assessed in 4,444 patients with. . .

Simvastatin is a lactone that is readily hydrolyzed in vivo to the corresponding beta-hydroxyacid, a potent inhibitor of HMG-CoA reductase. Inhibition. . . the beta-hydroxyacid metabolites (active inhibitors) and, following base hydrolysis, active plus latent inhibitors (total inhibitors) in plasma following administration of **simvastatin**.

Following an oral dose of 14C-labeled **simvastatin** in man, 13 percent of the dose was excreted in urine and 60 percent in feces. The latter represents absorbed drug equivalents excreted in bile, as well as any unabsorbed drug. Plasma concentrations of total radioactivity (**simvastatin** plus 14C-metabolites) peaked at 4 hours and declined rapidly to about 10 percent of peak by 12 hours postdose. Absorption of **simvastatin**, estimated relative to an intravenous reference dose, in each of two animal species tested, averaged about 85 percent of an oral dose. In animal studies, after oral dosing, **simvastatin** achieved substantially higher concentrations in the liver than in non-target tissues. **Simvastatin** undergoes extensive first-pass extraction in the liver, its primary site of action, with subsequent excretion of drug equivalents in the bile. As a consequence of extensive hepatic extraction of **simvastatin** (estimated to be greater than 60 percent in man), the availability of drug to the general circulation is low. In. . . a single-dose study in nine healthy subjects, it was estimated that less than 5 percent of an oral dose of **simvastatin** reaches the general circulation as active inhibitors. Following administration of **simvastatin** tablets, the coefficient of variation, based on between-subject variability, was approximately 48 percent for the area under the concentration-time curve. . .

Both **simvastatin** and its beta-hydroxyacid metabolite are highly bound (approximately 95 percent) to human plasma proteins. Animal studies have not been performed to determine whether **simvastatin** crosses the blood-brain and placental barriers. However, when radiolabeled **simvastatin** was administered to rats, **simvastatin**-derived radioactivity crossed the blood-brain barrier.

The major active metabolites of **simvastatin** present in human plasma are the beta-hydroxyacid of **simvastatin** and its 6c-hydroxy, 6c-hydroxymethyl, and 6c-exomethylene derivatives. Peak plasma concentrations of both active and total inhibitors were attained within 1.3. . . to as high as 120 mg. Relative to the fasting state, the plasma profile of inhibitors was not affected when **simvastatin** was administered immediately before an American Heart Association recommended low- fat meal.

The results of 3 separate studies depicting the dose response to **simvastatin** in patients with primary hypercholesterolemia are presented in TABLE 1.

In a controlled clinical study, 12 patients 15-39 years of age with

homozygous familial hypercholesterolemia received **simvastatin** 40 mg/day in a single dose or in 3 divided doses, or 80 mg/day in 3 divided doses. Eleven of. . .

In . . . significantly reduced by 42 percent, (p equals 0.00001, 111 vs 189). There was no statistically significant difference between groups in non-**cardiovascular** mortality. ZOCOR also significantly decreased the risk of having major coronary events (CHD mortality plus hospital-verified and silent non-fatal myocardial. . .

In the Multicenter Anti-Atheroma Study, the effect of therapy with **simvastatin** on atherosclerosis was assessed by quantitative coronary angiography in hypercholesterolemic men and women with coronary heart disease. In this randomized,. . . (6.4 mmol/L) and a mean baseline LDL-C value of 170 mg/dL (4.4 mmol/L) were treated with conventional measures and with **simvastatin** 20 mg/day or placebo. Angiograms were evaluated at baseline, two and four years. A total of 347 patients had a. . . endpoints of the trial were mean change per-patient in minimum and mean lumen diameters, indicating focal and diffuse disease, respectively. **Simvastatin** significantly slowed the progression of lesions as measured in the final angiogram by both these parameters (mean changes in minimum lumen diameter: _0.04 mm with **simvastatin** vs _0.12 mm with placebo; mean changes in mean lumen diameter: _0.03 mm with **simvastatin** vs _0.08 mm with placebo), as well as by change from baseline in percent diameter stenosis (0.9 percent **simvastatin** vs 3.6 percent placebo). After four years, the groups also differed significantly in the proportions of patients categorized with disease progression (23 percent **simvastatin** vs 33 percent placebo) and disease regression (18 percent **simvastatin** vs 12 percent placebo). In addition, **simvastatin** significantly decreased the proportion of patients with new lesions (13 percent **simvastatin** vs 24 percent placebo) and with new total occlusions (5 percent vs 11 percent). The mean change per-patient in. . .

In clinical studies, **simvastatin** did not impair adrenal reserve or significantly reduce basal plasma cortisol concentration. Small reductions from baseline in basal plasma testosterone in men were observed in clinical studies with **simvastatin**, an effect also observed with other inhibitors of HMG-CoA reductase and the bile acid sequestrant cholestyramine. There was no effect on plasma gonadotropin levels. In a placebo-controlled 12-week study there was no significant effect of **simvastatin** 80 mg on the plasma testosterone response to human chorionic gonadotropin (hCG). In another 24-week study, **simvastatin** 20-40 mg had no detectable effect on spermatogenesis. In 4S, in which 4,444 patients were randomized to **simvastatin** 20-40 mg or placebo daily for a median duration of 5.4 years, the incidence of male sexual adverse events in. . .

Prior to initiating therapy with **simvastatin**, secondary causes for hypercholesterolemia (e.g., poorly controlled diabetes mellitus, hypothyroidism, nephrotic syndrome, dysproteinemias, obstructive liver disease, other drug therapy, alcoholism). . .

Simvastatin and other inhibitors of HMG-CoA reductase occasionally cause myopathy, which is manifested as muscle pain or weakness associated with grossly. . . failure secondary to myoglobinuria, has been reported rarely. In 4S, there was one case of myopathy among 1,399 patients taking **simvastatin** 20 mg and no cases among 822 patients taking 40 mg daily for a median duration of 5.4 years. In. . .

In addition, the risk of myopathy appears to be increased by high levels of HMG-CoA reductase inhibitory activity in plasma. **Simvastatin** is metabolized by the cytochrome P450 isoform 3A4. Certain drugs which share this metabolic pathway can raise the plasma levels of **simvastatin** and may increase the risk of myopathy. These include cyclosporine, itraconazole, ketoconazole and other antifungal azoles, the macrolide antibiotics erythromycin. . .

1. General measures. Patients starting therapy with **simvastatin** should be advised of the risk of myopathy, and told to report promptly unexplained muscle pain, tenderness or weakness. A CK level above 10X ULN in a patient with unexplained muscle symptoms indicates myopathy. **Simvastatin** therapy should be discontinued if myopathy is diagnosed or suspected. In most cases, when patients were promptly discontinued from treatment,. . .

Of . . . patients, dose escalation requires caution. Also, as there are no known adverse consequences of brief interruption of therapy, treatment with **simvastatin** should be stopped a few days before elective major surgery and when any major acute medical or surgical condition supervenes.

2. . . . reduce the risk of myopathy caused by drug interactions (see above and PRECAUTIONS, Drug Interactions). Physicians contemplating combined therapy with **simvastatin** and any of the interacting drugs

should weigh the potential benefits and risks, and should carefully monitor patients for any. . .

The combined use of **simvastatin** with fibrates or niacin should be avoided unless the benefit of further alteration in lipid levels is likely to outweigh the increased risk of this drug combination. Combinations of fibrates or niacin with low doses of **simvastatin** have been used without myopathy in small, short-term clinical trials with careful monitoring. Addition of these drugs to **simvastatin** typically provides little additional reduction in LDL-C, but further reductions of TG and further increases in HDL-C may be obtained.. . .

one of these drugs must be used with **simvastatin**, clinical experience suggests that the risk of myopathy is less with niacin than with the fibrates.

In patients taking concomitant cyclosporine, fibrates or niacin, the dose of **simvastatin** should generally not exceed 10 mg (see DOSAGE AND ADMINISTRATION, General Recommendations and Concomitant Lipid-Lowering Therapy), as the risk of myopathy increases substantially at higher doses. Interruption of **simvastatin** therapy during a course of treatment with a systemic antifungal azole or a macrolide antibiotic should be considered.

Liver Dysfunction

Persistent increases (to more than 3X the ULN) in serum transaminases have occurred in approximately 1 percent of patients who received **simvastatin** in clinical trials. When drug treatment was interrupted or discontinued in these patients, the transaminase levels usually fell slowly to. . .

In . . . one transaminase elevation to greater than 3X ULN, over the course of the study, was not significantly different between the **simvastatin** and placebo groups (14 [0.7 percent] vs. 12 [0.6 percent]). Elevated transaminases resulted in the discontinuation of 8 patients from therapy in the **simvastatin** group (n equals 2,221) and 5 in the placebo group (n equals 2,223). Of the 1,986 **simvastatin** treated patients in 4S with normal liver function tests (LFTs) at baseline, only 8 (0.4 percent) developed consecutive LFT. . . abnormalities within the first year. All of the patients in this study received a starting dose of 20 mg of **simvastatin**; 37 percent were titrated to 40 mg.

The . . . have a past history of liver disease. Active liver diseases or unexplained transaminase elevations are contraindications to the use of **simvastatin**.

As with other lipid-lowering agents, moderate (less than 3X ULN) elevations of serum transaminases have been reported following therapy with **simvastatin**. These changes appeared soon after initiation of therapy with **simvastatin**, were often transient, were not accompanied by any symptoms and did not require interruption of treatment.

Simvastatin may cause elevation of CK and transaminase levels (see WARNINGS and ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with **simvastatin**.

Antipyrine: **Simvastatin** had no effect on the pharmacokinetics of antipyrine. However, since **simvastatin** is metabolized by the cytochrome P450 isoform 3A4, this does not preclude an interaction with other drugs metabolized by the. . .

Propranolol: In healthy male volunteers there was a significant decrease in mean Cmax, but no change in AUC, for **simvastatin** total and active inhibitors with concomitant administration of single doses of ZOCOR and **propranolol**. The clinical relevance of this finding is unclear. The pharmacokinetics of the enantiomers of **propranolol** were not affected.

Digoxin: Concomitant administration of a single dose of digoxin in healthy male volunteers receiving **simvastatin** resulted in a slight elevation (less than 0.3 ng/mL) in digoxin concentrations in plasma (as measured by a radioimmunoassay) compared to concomitant administration of placebo and digoxin. Patients taking digoxin should be monitored appropriately when **simvastatin** is initiated.

Warfarin: In two clinical studies, one in normal volunteers and the other in hypercholesterolemic patients, **simvastatin** 20-40 mg/day modestly potentiated the effect of coumarin anticoagulants: the prothrombin time, reported as International Normalized Ratio (INR), increased from. . . been reported in a few patients taking coumarin anticoagulants concomitantly. In such patients, prothrombin time should be determined before starting **simvastatin** and frequently enough during early therapy to insure that no significant alteration of prothrombin time occurs. Once a stable prothrombin. . . documented, prothrombin times can be monitored at the intervals usually recommended for patients on coumarin anticoagulants. If the dose of **simvastatin** is changed or discontinued, the same procedure should be repeated. **Simvastatin** therapy has not been associated with bleeding or with changes in prothrombin time

in patients not taking anticoagulants.

Optic nerve degeneration was seen in clinically normal dogs treated with **simvastatin** for 14 weeks at 180 mg/kg/day, a dose that produced mean plasma drug levels about 12 times higher than the. . .

CNS . . . mononuclear cell infiltration of perivascular spaces, perivascular fibrin deposits and necrosis of small vessels were seen in dogs treated with **simvastatin** at a dose of 360 mg/kg/day, a dose that produced mean plasma drug levels that were about 14 times higher. . .

In a 72-week carcinogenicity study, mice were administered daily doses of **simvastatin** of 25, 100, and 400 mg/kg body weight, which resulted in mean plasma drug levels approximately 1, 4, and 8. . .

In . . . evidence of a tumorigenic effect was observed (mean plasma drug levels were 1 times higher than humans given 80 mg **simvastatin** as measured by AUC).

In . . . significant increase in the incidence of thyroid follicular adenomas in female rats exposed to approximately 11 times higher levels of **simvastatin** than in humans given 80 mg **simvastatin** (as measured by AUC).

There was decreased fertility in male rats treated with **simvastatin** for 34 weeks at 25 mg/kg body weight (4 times the maximum human exposure level, based on AUC, in patients receiving 80 mg/day); however, this effect was not observed during a subsequent fertility study in which **simvastatin** was administered at this same dose level to male rats for 11 weeks (the entire cycle of spermatogenesis including epididymal. . .

Simvastatin was not teratogenic in rats at doses of 25 mg/kg/day or in rabbits at doses up to 10 mg/kg daily.. . .

It is not known whether **simvastatin** is excreted in human milk. Because a small amount of another drug in this class is excreted in human milk and because of the potential for serious adverse reactions in nursing infants, women taking **simvastatin** should not nurse their infants (see CONTRAINDICATIONS).

Safety . . . with this drug is limited (no studies in subjects below the age of 20 years), treatment of pediatric patients with **simvastatin** is not recommended at this time.

Scandinavian **Simvastatin** Survival Study

The . . . effects have been reported with drugs in this class. Not all the effects listed below have necessarily been associated with **simvastatin** therapy.

In controlled clinical studies in which **simvastatin** was administered concomitantly with cholestyramine, no adverse reactions peculiar to this concomitant treatment were observed. The adverse reactions that occurred were limited to those reported previously with **simvastatin** or cholestyramine. The combined use of **simvastatin** with fibrates should generally be avoided (see WARNINGS, Skeletal Muscle).

The dialyzability of **simvastatin** and its metabolites in man is not known at present.

In patients taking cyclosporine concomitantly with **simvastatin** (see WARNINGS, Skeletal Muscle), therapy should begin with 5 mg of ZOCOR and should not exceed 10 mg/day.

Tablets ZOCOR (**simvastatin**) 5 mg, 10 mg, 20 mg, and 40 mg are manufactured by:

Tablets ZOCOR (**simvastatin**) 80 mg are manufactured for:

*** Manson, J.M., Freyssinges, C., Ducrocq, MB., Stephenson, W.P., Postmarketing Surveillance of **Lovastatin** and **Simvastatin** Exposure During Pregnancy, Reproductive Toxicology, 10(6): 439-446, 1996.

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AB TABLETS
ZOCOR(R)
(**SIMVASTATIN**)
DESCRIPTION

ZOCOR* (**simvastatin**) is a lipid-lowering agent that is derived synthetically from a fermentation product of Aspergillus terreus. After oral ingestion, **simvastatin**, which is an inactive lactone, is hydrolyzed to the corresponding beta-hydroxyacid form. This is an inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyzes the conversion of HMG-CoA to mevalonate, which is an early and rate-limiting step in the biosynthesis of cholesterol.

Simvastatin is butanoic acid, 2,2-dimethyl-,1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)-ethyl]-1-naphthalenyl ester, [1S-[1alpha,3 alpha,7 beta,8 beta(2S*,4S*),-8a beta]]. The empirical formula of **simvastatin** is C25H38O5 and its molecular weight is 418.57. Its structural formula is:

(MOLECULE HERE)

Simvastatin is a white to off-white, nonhygroscopic, crystalline powder that is practically insoluble in water, and freely soluble in chloroform, methanol and ethanol.

Tablets ZOCOR for oral administration contain either 5 mg, 10 mg, 20 mg, 40 mg or 80 mg of **simvastatin** and the following inactive ingredients: cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, iron oxides, lactose, magnesium stearate, starch, talc, titanium dioxide and other ingredients. Butylated hydroxyanisole is added as a preservative.

CLINICAL PHARMACOLOGY

The involvement of low-density lipoprotein (LDL) cholesterol in atherogenesis has been well-documented in clinical and pathological studies, as well as in many animal experiments. Epidemiological studies have established that high LDL (low-density lipoprotein) cholesterol and low HDL (high-density lipoprotein) cholesterol are both risk factors for coronary heart disease. Though frequently found in association with low HDL, elevated plasma triglycerides (TG) have not been established as an independent risk factor for coronary heart disease. The independent effect of raising HDL or lowering TG on the risk of coronary and **cardiovascular** morbidity and mortality has not been determined.

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The . . . factor for coronary heart disease. The independent effect of raising HDL or lowering TG on the risk of coronary and **cardiovascular** morbidity and mortality has not been determined.

In the Scandinavian **Simvastatin** Survival Study (4S), the effect of improving lipoprotein levels with ZOCOR on total mortality was assessed in 4444 patients with. . .

Simvastatin is a lactone that is readily hydrolyzed in vivo to the

corresponding beta -hydroxyacid, a potent inhibitor of HMG-CoA reductase.. . . beta -hydroxyacid metabolites (active inhibitors) and, following base hydrolysis, active plus latent inhibitors (total inhibitors) in plasma following administration of **simvastatin**.

Following an oral dose of 14C-labeled **simvastatin** in man, 13 percent of the dose was excreted in urine and 60 percent in feces. The latter represents absorbed drug equivalents excreted in bile, as well as any unabsorbed drug. Plasma concentrations of total radioactivity (**simvastatin** plus 14C-metabolites) peaked at 4 hours and declined rapidly to about 10 percent of peak by 12 hours postdose. Absorption of **simvastatin**, estimated relative to an intravenous reference dose, in each of two animal species tested, averaged about 85 percent of an oral dose. In animal studies, after oral dosing, **simvastatin** achieved substantially higher concentrations in the liver than in non-target tissues. **Simvastatin** undergoes extensive first-pass extraction in the liver, its primary site of action, with subsequent excretion of drug equivalents in the bile. As a consequence of extensive hepatic extraction of **simvastatin** (estimated to be greater than 60 percent in man), the availability of drug to the general circulation is low. In. . . a single-dose study in nine healthy subjects, it was estimated that less than 5 percent of an oral dose of **simvastatin** reaches the general circulation as active inhibitors. Following administration of **simvastatin** tablets, the coefficient of variation, based on between-subject variability, was approximately 48 percent for the area under the concentration-time curve. . .

Both **simvastatin** and its beta-hydroxyacid metabolite are highly bound (approximately 95 percent) to human plasma proteins. Animal studies have not been performed to determine whether **simvastatin** crosses the blood-brain and placental barriers. However, when radiolabeled **simvastatin** was administered to rats, **simvastatin**-derived radioactivity crossed the blood-brain barrier.

The major active metabolites of **simvastatin** present in human plasma are the beta-hydroxyacid of **simvastatin** and its 6 prime-hydroxy, 6 prime- hydroxymethyl, and 6 prime-exomethylene derivatives. Peak plasma concentrations of both active and total inhibitors. . . to as high as 120 mg. Relative to the fasting state, the plasma profile of inhibitors was not affected when **simvastatin** was administered immediately before an A.H.A. recommended low-fat meal.

The results of 3 separate studies depicting the dose response to **simvastatin** in patients with primary hypercholesterolemia are presented in TABLE I.

In a controlled clinical study, 12 patients 15-39 years of age with homozygous familial hypercholesterolemia received **simvastatin** 40 mg/day in a single dose or in 3 divided doses, or 80 mg/day in 3 divided doses. Eleven of. . .

In the Scandinavian **Simvastatin** Survival Study (4S), the effect of therapy with ZOCOR on total mortality was assessed in 4444 patients with coronary heart. . . reduced by 42 percent, (p equals 0.00001, 111 vs 189). There was no statistically significant difference between groups in non- **cardiovascular** mortality. ZOCOR also significantly decreased the risk of having major coronary events (CHD mortality plus hospital-verified and silent non-fatal myocardial. . .

In the Multicenter Anti-Atheroma Study, the effect of therapy with **simvastatin** on atherosclerosis was assessed by quantitative coronary angiography in hypercholesterolemic men and women with coronary heart disease. In this randomized,. . . (6.4 mmol/L) and a mean baseline LDL value of 170 mg/dL (4.4 mmol/L) were treated with conventional measures and with **simvastatin** 20 mg/day or placebo. Angiograms were evaluated at baseline, two and four years. A total of 347 patients had a. . . endpoints of the trial were mean change per-patient in minimum and mean lumen diameters, indicating focal and diffuse disease, respectively. **Simvastatin** significantly slowed the progression of lesions as measured in the final angiogram by both these parameters (mean changes in minimum lumen diameter: negative 0.04 mm with **simvastatin** vs negative 0.12 mm with placebo; mean changes in mean lumen diameter: negative 0.03 mm with **simvastatin** vs negative 0.08 mm with placebo), as well as by change from baseline in percent diameter stenosis (0.9 percent **simvastatin** vs 3.6 percent placebo). After four years, the groups also differed significantly in the proportions of patients categorized with disease progression (23 percent **simvastatin** vs 33 percent placebo) and disease regression (18 percent **simvastatin** vs 12 percent placebo). In addition, **simvastatin** significantly decreased the proportion of patients with new lesions (13 percent **simvastatin** vs 24 percent placebo) and with new total occlusions (5 percent vs 11 percent). The mean change per-patient in mean. . .

In clinical studies, **simvastatin** did not impair adrenal reserve or significantly reduce basal plasma cortisol concentration. Small reductions from baseline in basal plasma testosterone in men were observed in clinical studies with **simvastatin**, an effect also observed with other inhibitors of HMG-CoA reductase and the bile acid sequestrant cholestyramine. There was no effect on plasma gonadotropin levels. In a placebo-controlled 12-week study there was no significant effect of **simvastatin** 80 mg on the plasma testosterone response to hCG. In another 24-week study **simvastatin** 20-40 mg had no detectable effect on spermatogenesis. In 4S, in which 4444 patients were randomized to **simvastatin** 20-40 mg or placebo daily for a median duration of 5.4 years, the incidence of male sexual adverse events in. . .

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Simvastatin and other inhibitors of HMG-CoA reductase occasionally cause myopathy, which is manifested as muscle pain or weakness associated with grossly. . . of normal [ULN]). Rhabdomyolysis, with or without acute renal failure secondary to myoglobinuria, has been reported rarely. In the Scandinavian **Simvastatin** Survival Study, there was one case of myopathy among 1399 patients taking **simvastatin** 20 mg and no cases among 822 patients taking 40 mg daily for a median duration of 5.4 years. In. .

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In addition, the risk of myopathy appears to be increased by high levels of HMG-CoA reductase inhibitory activity in plasma. **Simvastatin** is metabolized by the cytochrome P450 isoform 3A4. Certain drugs which share this metabolic pathway can raise the plasma levels of **simvastatin** and may increase the risk of myopathy. These include cyclosporine, itraconazole, ketoconazole and other antifungal azoles, the macrolide antibiotics erythromycin. . .

1. General measures. Patients starting therapy with **simvastatin** should be advised of the risk of myopathy, and told to report promptly unexplained muscle pain, tenderness or weakness. A creatine kinase (CK) level above 10X ULN in a patient with unexplained muscle symptoms indicates myopathy. **Simvastatin** therapy should be discontinued if myopathy is diagnosed or suspected. In most cases, when patients were promptly discontinued from treatment,. . .

Of . . . patients, dose escalation requires caution. Also, as there are no known adverse consequences of brief interruption of therapy, treatment with **simvastatin** should be stopped a few days before elective major surgery and when any major acute medical or surgical condition supervenes.

2. . . . reduce the risk of myopathy caused by drug interactions (see above and PRECAUTIONS, Drug Interactions). Physicians contemplating combined therapy with **simvastatin** and any of the interacting drugs should weigh the potential benefits and risks, and should carefully monitor patients for any. . .

The combined use of **simvastatin** with fibrates or niacin should be avoided unless the benefit of further alteration in lipid levels is likely to outweigh the increased risk of this drug combination. Combinations of fibrates or niacin with low doses of **simvastatin** have been used without myopathy in small, short-term clinical trials with careful monitoring. Addition of these drugs to **simvastatin** typically provides little additional reduction in LDL cholesterol, but further reductions of triglycerides and further increases in HDL cholesterol may be obtained. If one of these drugs must be used with **simvastatin**, clinical experience suggests that the risk of myopathy is less with niacin than with the fibrates.

In patients taking concomitant cyclosporine, fibrates or niacin, the dose of **simvastatin** should generally not exceed 10 mg (see DOSAGE AND ADMINISTRATION, General Recommendations and Concomitant Lipid-Lowering Therapy), as the risk of myopathy increases substantially at higher doses. Interruption of **simvastatin** therapy during a course of treatment with a systemic antifungal azole or a macrolide antibiotic should be considered.

Persistent . . . 3 times the upper limit of normal) in serum transaminases have occurred in approximately 1 percent of patients who received **simvastatin** in clinical trials. When drug treatment was interrupted or discontinued in these patients, the transaminase levels usually fell slowly to. . . were not associated with jaundice or other clinical signs or symptoms. There was no evidence of hypersensitivity. In the Scandinavian **Simvastatin** Survival Study (see CLINICAL PHARMACOLOGY, Clinical Studies), the number of patients with more than one transaminase elevation to greater than 3 times the upper limit of normal, over the course of the study, was not significantly different between the **simvastatin** and placebo groups (14 [0.7 percent] vs. 12 [0.6 percent]).

Elevated transaminases resulted in the discontinuation of 8 patients from therapy in the **simvastatin** group (n equals 2,221) and 5 in the placebo group (n equals 2,223). Of the 1986 **simvastatin** treated patients in 4S with normal liver function tests (LFTs) at baseline, only 8 (0.4 percent) developed consecutive LFT elevations. . . abnormalities within the first year. All of the patients in this study received a starting dose of 20 mg of **simvastatin**; 37 percent were titrated to 40 mg. In 2 controlled clinical studies in 1105 patients, the 12-month incidence of persistent. . .

The . . . have a past history of liver disease. Active liver diseases or unexplained transaminase elevations are contraindications to the use of **simvastatin**.

As . . . moderate (less than three times the upper limit of normal) elevations of serum transaminases have been reported following therapy with **simvastatin**. These changes appeared soon after initiation of therapy with **simvastatin**, were often transient, were not accompanied by any symptoms and did not require interruption of treatment.

Simvastatin may cause elevation of creatine kinase and transaminase levels (see WARNINGS and ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with **simvastatin**.

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Safety . . . with this drug is limited (no studies in subjects below the age of 20 years), treatment of pediatric patients with **simvastatin** is not recommended at this time.

Scandinavian **Simvastatin** Survival Study

In the Scandinavian **Simvastatin** Survival Study (4S) (see CLINICAL PHARMACOLOGY, Clinical Studies) involving 4444 patients treated with 20-40 mg/day of ZOCOR (n equals 2221). . .

The . . . effects have been reported with drugs in this class. Not all the effects listed below have necessarily been associated with **simvastatin** therapy.

In controlled clinical studies in which **simvastatin** was administered concomitantly with cholestyramine, no adverse reactions peculiar to this concomitant treatment were observed. The adverse reactions that occurred were limited to those reported previously with **simvastatin** or cholestyramine. The combined use of **simvastatin** with fibrates should generally be avoided (see WARNINGS, Skeletal Muscle).

A . . . 450 mg. Until further experience is obtained, no specific treatment of overdosage with ZOCOR can be recommended. The dialyzability of **simvastatin** and its metabolites in man is not known at present.

In patients taking cyclosporine concomitantly with **simvastatin** (see WARNINGS, Skeletal Muscle), therapy should begin with 5 mg of ZOCOR and should not exceed 10 mg/day.

Tablets ZOCOR (**simvastatin**) 5 mg, 10 mg, 20 mg, and 40 mg are manufactured by:

Tablets ZOCOR (**simvastatin**) 80 mg are manufactured for:

*** Manson, J.M., Freyssinges, C., Ducrocq, M.B., Stephenson, W.P., Postmarketing Surveillance of **Lovastatin** and **Simvastatin** Exposure During Pregnancy, Reproductive Toxicology, 10(6):439-446, 1996.

L15 ANSWER 3 OF 192 DRUGU COPYRIGHT 2001 DERWENT INFORMATION LTD
Full-text
ACCESSION NUMBER: 1998-23905 DRUGU T
TITLE: Selection of drug therapy in stable angina pectoris.
AUTHOR: Savonitto S; Ardissino D
CORPORATE SOURCE: Univ.Pavia
LOCATION: Milan; Pavia, It.
SOURCE: Cardiovasc.Drugs Ther. (12, No. 2, 197-210, 1998) 3 Fig. 3 Tab. 107 Ref.
CODEN: CDTHET ISSN: 0920-3206
AVAIL. OF DOC.: Seconda Divisione Cardiologica, Ospedale Niguarda Ca' Granda, 20162 Milano, Italy. (e-mail: ssavoni@tin.it).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 1998-23905 DRUGU T
AB The selection of drug therapy in stable angina pectoris is reviewed with respect to etiology of effort angina, aims of treatment, medical therapy for the prevention of mortality and major cardiac events, anti-ischemic therapy, drug selection, combination anti-ischemic therapy, silent ischemia and conduct of anti-ischemic therapy in individual patients. Drugs reported include aspirin, **simvastatin**, **atenolol**, **metoprolol**, verapamil, nifedipine, pravastatin, isradipine, **propranolol**, felodipine, nitroglycerin and amlodipine. Treatment of stable angina should prevent myocardial infarction, cardiac death and prevent anginal attacks. Anginal symptoms are not considered useful for selection of drug therapy. Evaluation of patients, including consideration of drug contraindications, concomitant diseases and side-effects should be combined with a more individualized approach.
ABEX The physician needs to decide whether to treat the patient with medicine or a revascularization procedure, such as PTCA or coronary artery by-pass grafting. There is no superiority of revascularization over therapy. Several prospective, randomized trials have been completed in patients with stable coronary artery disease. Lipid-lowering therapy in primary prevention of cardiac events has been confirmed. None of the anti-ischemic drugs have yet been tested enough for the potential of primary preventive effect in stable angina. Data exists on primary and secondary prevention of cardiac events in patients with hypertension and those with a recent myocardial infarction. From these studies, a primary preventive effect in stable angina may be logical, but has not been

proven. Some agents have been shown to decrease anginal symptoms and increase exercise tolerance acting through multiple mechanisms. Exercise data provides useful information for selecting initial treatment. The hyperventilation test is a useful method of testing increased coronary vasomotor tone and may be helpful in the selection of initial therapy. Most patients are treated with combination treatment as combining an agent that decreases oxygen consumption with 1 that increases coronary blood flow should lead to optimal delivery, use of oxygen, raised exercise tolerance and fewer anginal symptoms. An additive effect of combination therapy is discussed. Ambulatory electrocardiographic monitoring is not necessary as a way of selecting beneficial therapy. (FD)

CT ANGINA-PECTORIS *TR; STABLE *TR; **CARDIOPATHY** *TR; CORONARY-DISEASE *TR; REVIEW *FT; CASES *FT; IN-VIVO *FT; HYPOTENSIVE *FT; CARDIANT *FT; ANTIAGGREGANT *FT

CT ANGINA-PECTORIS *TR; STABLE *TR; **CARDIOPATHY** *TR; CORONARY-DISEASE *TR; REVIEW *FT; CASES *FT; IN-VIVO *FT; HYPOTENSIVE *FT; CARDIANT *FT; ANTIAGGREGANT *FT

[02] ASPIRIN *TR; **SIMVASTATIN** *TR; PRAVASTATIN *TR; **ATENOLOL** *TR; **METOPROLOL** *TR; VERAPAMIL *TR; NIFEDIPINE *TR; ISRADIPINE *TR; **PROPRANOLOL** *TR; FELODIPINE *TR; NITROGLYCEROL *TR; AMLODIPINE *TR; TR *FT

L15 ANSWER 4 OF 192 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 92177255 EMBASE
DOCUMENT NUMBER: 1992177255
TITLE: **Lovastatin** and coadministered antihypertensive/**cardiovascular** agents.
AUTHOR: Pool J.L.; Shear C.L.; Downton M.; Schnaper H.; Stinnett S.; Dujovne C.; Bradford R.H.; Chremos A.N.
CORPORATE SOURCE: Methodist Hospital, Mail Station F-504, 6535 Fannin Street,Houston, TX 77030, United States
SOURCE: Hypertension, (1992) 19/3 (242-248).
ISSN: 0194-911X CODEN: HPRTDN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Hypertension and hypercholesterolemia frequently coexist and may require concomitant drug treatments. The efficacy and safety profile of **lovastatin** given in the presence of antihypertensive medication was evaluated using patient subgroups identified in the Expanded Clinical Evaluation of **Lovastatin** (EXCEL) Study. The EXCEL study examined 8,245 patients with moderate hypercholesterolemia randomly assigned either to a group treated with **lovastatin** (20-80 mg daily) or to a group given placebo for 48 weeks. After adjustment for patient characteristics, pairwise comparisons were made between patients taking no antihypertensive agents (n=3,772) and those taking either calcium antagonists (n=446), selective .beta.1-adrenergic receptor blockers (n=326), nonselective .beta.-adrenergic receptor blockers (n=219), potassium-sparing diuretics (n=187), thiazide diuretics (n=126), or angiotensin converting enzyme inhibitors (n=171). The placebo-corrected dose- dependent effect of **lovastatin** on the percent change from baseline in low- density lipoprotein cholesterol was not attenuated in any subgroup and was slightly enhanced in the calcium antagonist subgroup (-29% to -44%, p=0.06) when compared with patients taking no antihypertensive agents (-24% to -40%); this difference, however, was only of borderline significance. Patterns of **lovastatin**-induced increase in high-density lipoprotein cholesterol and decrease in triglycerides were not consistently different among the subgroups. Examination of mean changes in serum transaminases, mean changes in creatine kinase, and the proportion of patients discontinuing therapy for clinical adverse experiences did not indicate the presence of an interaction. In conclusion, there was no evidence for an attenuation of the **lovastatin**- induced changes in lipids and lipoproteins or of an alteration in the safety profile of **lovastatin** when administered concurrently with commonly used antihypertensive agents.

CT Medical Descriptors:
*hypercholesterolemia: . . . level
*antihypertensive agent: PD, pharmacology
*antihypertensive agent: CM, drug comparison
*antihypertensive agent: CB, drug combination
*antihypertensive agent: IT, drug interaction

*antihypertensive agent: DT, drug therapy
***cardiovascular agent: PD, pharmacology**
***cardiovascular agent: DT, drug therapy**
***cardiovascular agent: IT, drug interaction**
***cardiovascular agent: CB, drug combination**
***cardiovascular agent: CM, drug comparison**
*mevinolin: CM, drug comparison
*mevinolin: IT, drug interaction
*mevinolin: CB, drug combination
*mevinolin: DO, drug dose
*mevinolin: PD, pharmacology
*mevinolin: DT, drug therapy
amiloride: PD, pharmacology
amiloride: DT, drug therapy
amiloride: CB, drug combination
amiloride: CM, drug comparison
amiloride: IT, drug interaction
atenolol: CB, drug combination
atenolol: CM, drug comparison
atenolol: DT, drug therapy
atenolol: IT, drug interaction
atenolol: PD, pharmacology
diltiazem: CB, drug combination
diltiazem: CM, drug comparison
diltiazem: PD, pharmacology
diltiazem: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: CM, drug comparison
dipeptidyl carboxypeptidase inhibitor:. . . therapy
labetalol: CB, drug combination
labetalol: PD, pharmacology
labetalol: DT, drug therapy
labetalol: IT, drug interaction
labetalol: CM, drug comparison
low density lipoprotein cholesterol: EC, endogenous compound
metoprolol: PD, pharmacology
metoprolol: IT, drug interaction
metoprolol: CM, drug comparison
metoprolol: CB, drug combination
metoprolol: DT, drug therapy
nadolol: PD, pharmacology
nadolol: DT, drug therapy
nadolol: IT, drug interaction
nadolol: CM, drug comparison
nadolol: CB, drug combination
nifedipine: PD, pharmacology
nifedipine: CB, drug combination
nifedipine: CM, drug comparison
nifedipine: IT, drug interaction
nifedipine: DT, drug therapy
propranolol: IT, drug interaction
propranolol: DT, drug therapy
propranolol: CB, drug combination
propranolol: PD, pharmacology
propranolol: CM, drug comparison
timolol: CB, drug combination
timolol: CM, drug comparison
timolol: IT, drug interaction
timolol: PD, pharmacology
timolol: DT, drug therapy
triacylglycerol: EC, endogenous compound
triamterene:. . .
RN (mevinolin) 75330-75-5; (amiloride) 2016-88-8, 2609-46-3; (**atenolol**) 29122-68-7; (diltiazem) 33286-22-5, 42399-41-7; (hydrochlorothiazide) 58-93-5; (labetalol) 32780-64-6, 36894-69-6; (**metoprolol**) 37350-58-6; (nadolol) 42200-33-9; (nifedipine) 21829-25-4; (**propranolol**) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (timolol) 26839-75-8; (triamterene) 396-01-0; (verapamil) 152-11-4, 52-53-9

L15 ANSWER 5 OF 192 ADISNEWS COPYRIGHT 2001 (ADIS)
Full-text
ACCESSION NUMBER: 1998:289 ED: 8 Aug 2001 UP: 8 Aug 2001
DOCUMENT NUMBER: 11738324-800632111
TITLE: Symposia: **Cerivastatin** stabilises plaques and has few drug interactions.

SOURCE: INPHARMA 3 Jul 1998 ISSN: 1173-8324
DOCUMENT TYPE: (MIX)
WORD COUNT: 1098
TI Symposia: **Cerivastatin** stabilises plaques and has few drug interactions.
TX. . . atherosclerotic plaque regression, but to the stabilisation of rupture- prone atherosclerotic lesions. Administration of the new HMG CoA reductase inhibitor **cerivastatin** decreases the lesional concentrations of collagen degrading enzymes and actually increases collagen levels in rupture-prone lesions. The lipid-lowering efficacy and tolerability of **cerivastatin** are broadly similar to those of other statins, but the drug is distinguished by a dual route of metabolic elimination. . . drug interaction profile. These factors may be points of differentiation for the agent over other available statins. A summary of **cerivastatin**'s pharmacological and clinical effects were presented at the 13th World Congress of **Cardiology** [Rio de Janeiro, Brazil; April 1998].

The traditional concept of atherosclerosis is one of progressive plaque growth in the coronary arteries.. . . by increasing the collagen content of unstable atherosclerotic plaques and stabilising the lesions, rather than by causing plaque regression.
Administration of **cerivastatin** to hypercholesterolaemic rabbits with experimentally induced atherosclerotic lesions resulted in reduced accumulation of macrophages and collagen-degrading enzymes in the lesions, said Dr Libby. In addition, the collagen content of the lesions was increased, resulting in increased lesional stability. **Cerivastatin** is the first statin for which this type of study has been conducted.
A highly potent statin
Cerivastatin is a fully synthetic third-generation statin, and the first drug in its class to be active in sub-milligram dosages.
Cerivastatin 0.1-0.4 mg/day reduced LDL-cholesterol levels by 22-36% in patients with moderate-to-severe hypercholesterolaemia (mean baseline LDL-cholesterol levels about 200 mg/dl),. . . pooled efficacy data presented by Dr Evan Stein from Medical Research Laboratories, Highland Heights, Kentucky, US. In one placebo-controlled study, **cerivastatin** 0.8 mg/day reduced LDL-cholesterol levels by 44% in patients with a mean baseline LDL-cholesterol level of 175 mg/dl. In contrast, LDL-cholesterol levels increased by 1.2% in placebo recipients. Thus, as with other statins, **cerivastatin** produced a log-linear dose-response curve. This means that there is approximately a 6% additional decrease in mean LDL-cholesterol levels for each doubling of the daily dose, with no plateau effect noted at the highest dosage yet tested [see table].
Cerivastatin therapy increases HDL-cholesterol levels by 4-8%. This effect, consistent with that of other statins, is not dose-related.
The triglyceride (TG)-lowering effects of **cerivastatin** are dependent on the patient's baseline TG level, according to Dr Stein. Modest reductions are seen in patients with low. . . mg/dl), and larger, dose-dependent, reductions occur in patients with baseline levels > 250 mg/dl.
Efficacy comparable with other statins
The effects of **cerivastatin** 0.2 and 0.3 mg/day were compared with those of fluvastatin 20 and 40 mg/day in a randomised, double-blind trial conducted. . . patients initially received placebo for a 6-week, single-blind, run-in period before being randomised to treatment.
After 6 weeks' therapy, recipients of **cerivastatin** 0.2 mg/day had significantly greater reductions in TGs and LDL- and total cholesterol levels accompanied by greater increases in HDL-cholesterol. . . with recipients of fluvastatin 20 mg/day ($p < 0.05$ for all comparisons). After a further 6 weeks of treatment with **cerivastatin** 0.3 mg/day or fluvastatin 40 mg/day, **cerivastatin** recipients were again observed to have superior responses in all comparisons ($p < 0.05$).
Good tolerability profile
According to Dr Stein, the pooled analysis data demonstrate that **cerivastatin** is well tolerated. The most common adverse events noted in studies with **cerivastatin** (headache, dyspepsia, flatulence, abdominal pain and diarrhoea) occurred in < 2% of patients, and in similar proportions for recipients of placebo and **cerivastatin**. The incidence of elevations in hepatic transaminase levels among **cerivastatin** recipients was similar to that observed with other statins.
Drug interactions unlikely
The drug-drug interaction profiles of other currently available statins are heterogenous. Antacids, cimetidine, cyclosporin, warfarin, **propranolol** and digoxin, among other agents, have all been shown to interact with various statins. However, unlike other statins, **cerivastatin** has a dual metabolic pathway, reported Dr Wolfgang Muck of Bayer AG, Wuppertal, Germany. **Cerivastatin** undergoes biotransformation to 2 major metabolites via the cytochrome P450 isozymes 2C8 and 3A4. These

pathways are compensatory, allowing the elimination of **cerivastatin** to be relatively unaffected by the presence of competing drugs, including erythromycin, itraconazole, nifedipine, warfarin and digoxin.
Additionally, **cerivastatin** does not affect the metabolism of these agents, he added.
Cerivastatin absorption is also unaffected by the presence of magnesium-aluminium antacids or the concomitant administration of cimetidine and omeprazole. However, cholestyramine does reduce **cerivastatin** absorption, but the interaction is clinically insignificant when administration of the 2 agents is separated by >= 1 hour.
Although the **cerivastatin** is highly bound to plasma proteins (> 99%), primarily albumin, its concomitant administration does not affect the pharmacokinetic profile of warfarin, nor does it alter the effects of warfarin on prothrombin time and factor VII.
Editorial Comment: **Cerivastatin** was launched in its first market the UK in April last year. It is now also available in several other. . .
Germany, The Netherlands, Sweden and Canada, and will be launched in more than 30 countries this year.

Table. Dose-response effect of **cerivastatin** in patients with moderate-to- severe hypercholesterolaemia

Cerivastatin dose	Percent reduction in LDL-cholesterol levels
0.1mg (n = 384)*	-22.4
0.2mg (n = 403)*	- 28.2
0.3mg (n =. . .	

RN 57-88-5 (CHOLESTEROL)
81-81-2 (WARFARIN)
114-07-8 (ERYTHROMYCIN)
525-66-6 (**PROPRANOLOL**)
9001-26-7 (PROTHROMBIN)
9031-66-7 (TRANSAMINASE)
11041-12-6 (CHOLESTYRAMINE)
20830-75-5 (DIGOXIN)
21829-25-4 (NIFEDIPINE)
51481-61-9 (CIMETIDINE)
73590-58-6 (OMEPRAZOLE)
84625-61-6 (ITRACONAZOLE)
93957-54-1 (FLUVASTATIN)
145599-86-6 (**CERIVASTATIN**)
9028-35-7Q, 37250-24-1Q (HMG-COA REDUCTASE)
59865-13-3Q, 79217-60-0Q (CYCLOSPORIN)

=> d ibib abs kwic 6-10

L15 ANSWER 6 OF 192 DRUGU COPYRIGHT 2001 DERWENT INFORMATION LTD
Full-text
ACCESSION NUMBER: 1995-43114 DRUGU T
TITLE: Beta-blockers and sudden cardiac death.
AUTHOR: Kendall M J; Lynch K P; Hjalmarson A; Kjekshus J
CORPORATE SOURCE: Univ.Oslo
LOCATION: Birmingham, U.K., Gothenburg, Swed.; Oslo, Nor.
SOURCE: Ann.Intern.Med. (123, No. 5, 358-67, 1995) 5 Fig. 2 Tab. 113 Ref.
CODEN: AIMEAS ISSN: 0003-4819
AVAIL. OF DOC.: Clinical Pharmacology Section, Department of Medicine, Queen Elizabeth Hospital, Birmingham M15 2TH, England.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 1995-43114 DRUGU T
AB The role of beta (b)-blockers in preventing sudden cardiac death is reviewed. Sudden cardiac death accounts for about 50% of cardiac mortality and the most common cause of cardiac death is ventricular arrhythmia as a consequence of coronary artery disease (CAD). Large, long-term trials have demonstrated consistent efficacy of b-blockers as **cardioprotective** agents, both alleviating myocardial ischemia and suppressing ventricular tachycardia. All b-blockers produce beneficial effects on myocardial ischemia and cardiac sympathetic activation but only the lypophilic, CNS-active b-blockers (such as timolol, **propranolol** and **metoprolol**) are **cardioprotective**, an effect attributed to attenuation of stress-induced vagal withdrawal; the

hydrophilic sotalol and **atenolol** lack efficacy.

ABEX Diuretic therapy for hypertension reduces coronary events in the elderly, but **metoprolol** is more effective than thiazide diuretics in reducing mortality. Aspirin and related drugs reduce post-MI mortality but not sudden cardiac death, whereas b-blockers reduce post-MI total mortality by about 20% and sudden cardiac death by 32-50%. Ca channel blockers have inconclusive or, for diltiazem, detrimental effects on mortality. ACE-inhibitors reduce post-MI **cardiovascular** death, but mainly in patients with impaired cardiac function, and magnesium or nitrates do not improve mortality. Animal studies indicate that some b-blockers (timolol, pindolol, **propranolol**, **metoprolol** and labetalol) increase the arrhythmia threshold. Encainide, flecainide, moricizine, quinidine and mexiletine may increase post-MI late mortality, but amiodarone appears to reduce mortality. **Simvastatin** is reported to reduce mortality in hypercholesterolemia/CAD. Nethalide, a b-blocker developed for hypertension, limits myocardial contractility in response to adrenalin and may cause or exacerbate CHF, but controlled studies have not demonstrated that **cardioselective** b-blockers increase CHF; in 1 study, **metoprolol** reduced use of furosemide for pulmonary edema. b-Blockers are contra-indicated in bronchospastic disease or **cardiogenic** shock, but are often witheld unnecessarily because of age, diabetes or CHF (where benefits may outweigh risks). Reports of adverse effects of b-blockers on well-being are generally anecdotal or unconfirmed (attributable to **propranolol** + methyldopa in some cases). (W2/LJ)

CT FIBRILLATION *TR; MYOCARD.INFARCT. *TR; CORONARY-DISEASE *TR; VENTRICULAR *TR; ARRHYTHMIA *TR; **CARDIOPATHY** *TR; CASES *FT; IN-VIVO *FT; REVIEW *FT; **CARDIOPROTECTIVE** *FT; SYMPATHOLYTIC-BETA *FT

[02] TIMOLOL *TR; **PROPRANOLOL** *TR; **METOPROLOL** *TR; SOTALOL *TR; **ATENOLOL** *TR; PINDOLOL *TR; LABETALOL *TR; TR *FT

L15 ANSWER 7 OF 192 DRUGU COPYRIGHT 2001 DERWENT INFORMATION LTD

Full-text

ACCESSION NUMBER: 1992-38640 DRUGU P T S

TITLE: Effects of a New Metabolic Modulator, Ranolazine, on Exercise Tolerance in Angina Pectoris Patients Treated with Beta-Blocker or Diltiazem.

AUTHOR: Cocco G; Rousseau M F; Bouvy T; Cheron P; Williams G; Detry J M

LOCATION: Rheinfelden, Switzerland; Brussels, Haine St Paul, Belgium; Leeds, United Kingdom

SOURCE: J.Cardiovasc.Pharmacol. (20, No. 1, 131-38, 1992) 2 Fig. 5 Tab. 15 Ref.

CODEN: JCPCDT ISSN: 0160-2446

AVAIL. OF DOC.: University of Louvain, avenue Hippocrate 55/5560, B-1200 Brussels, Belgium. (Pouleur H, 7 authors).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT; MPC

FILE SEGMENT: Literature

AN 1992-38640 DRUGU P T S

AB The effects of a single p.o. dose of ranolazine (RZ) were assessed in 104 patients with coronary artery disease and chronic stable angina pectoris in a double-blind, crossover, randomized, placebo-controlled study. All remained symptomatic despite treatment with diltiazem (DZ), **atenolol** (AT), **metoprolol** (ME) and **propranolol** (PR). Short acting nitrates, antiplatelet drugs and hypolipemic drugs (such as **simvastatin**) were allowed. The highest dose of RZ improved exercise duration, time to angina and time to 1 mm ST-segment depression. RZ did not affect HR or arterial pressure at rest and at peak exercise. Side effects were mild headache, dizziness and fatigue. A single dose of 240 mg RZ has an antianginal effect in patients already receiving a beta-blocker or DZ.

ABEX Methods 106 Patients (81 men; 28-73 yr, median 59) with coronary artery disease and chronic stable exercise-evoked angina receiving AT (100 mg/day), ME (200 mg/day), PR (120 mg/day) or DZ (60 mg t.i.d.) received a single p.o. dose of RZ (10, 60, 120 or 240 mg). Plasma RZ levels were measured by HPLC. Results 2 Patients were excluded. RZ (240 mg) increased exercise duration. "Intention-to-treat" analysis of time to angina showed an increase at 240 mg RZ, from 387 to 428 sec. Analysis of time to angina showed an increase on RZ (240 mg) of 56.8 sec. The effect was consistent in patients receiving DZ or beta-blockers (52 and 62 sec, respectively). Time to angina improved by at least 30 sec in 72% treated with 240 mg, 50% treated with 120 mg, 42% treated with 60 mg and 25% treated with 10 mg RZ. Time to 0.1 mV ST segment depression

increased with RZ (240 mg) by a mean of 36.5 and 43 sec when patients not achieving 0.1 min on both study days were excluded and included, respectively. RZ had no effect on resting or peak exercise HR, or systolic or diastolic B.P. values. Exercise was stopped due to angina in 54%, 62%, 59% and 32% at 10, 60, 120 and 240 mg RZ, respectively. Plasma RZ levels were higher in the DZ group than the beta-blocker group. There was a nonlinear relationship between log dose and plasma level of RZ. Angina was improved and summed ST segment depression reduced at plasma levels above 500 ng/ml. RZ induced symptoms such as mild headache, fatigue or dizziness in 22 patients. (E67/AE)

CT CHRON. *TR; STABLE *TR; ANGINA-PECTORIS *TR; **CARDIOPATHY** *TR; CORONARY-DISEASE *TR; **SIMVASTATIN** *RC; DRUG-COMPARISON *FT; IN-VIVO *FT; CASES *FT; COMB. *FT; RANDOM *FT; DOUBLE *FT; BLIND-TEST *FT; CLIN.TRIAL *FT; SYMPTOMATOLOGY *FT; CROSSOVER. . .

[03] **ATENOLOL** *TR; SYMPATHOLYTICS-BETA *FT; HYPOTENSIVES *FT; **ATENOLOL** *RN; TR *FT

[04] **METOPROLOL** *TR; SYMPATHOLYTICS-BETA *FT; METOPROLO *RN; TR *FT

[05] **PROPRANOLOL** *TR; SYMPATHOLYTICS-BETA *FT; ANTIARRHYTHMICS *FT; HYPOTENSIVES *FT; PROPRANOL *RN; TR *FT

[04] **METOPROLOL** *TR; SYMPATHOLYTICS-BETA *FT; METOPROLO *RN; TR *FT

[05] **PROPRANOLOL** *TR; SYMPATHOLYTICS-BETA *FT; ANTIARRHYTHMICS *FT; HYPOTENSIVES *FT; PROPRANOL *RN; TR *FT

[05] **PROPRANOLOL** *TR; SYMPATHOLYTICS-BETA *FT; ANTIARRHYTHMICS *FT; HYPOTENSIVES *FT; PROPRANOL *RN; TR *FT

DDRN RANOLAZIN; DILTIAZEM; METOPROLO; **ATENOLOL**; PROPRANOL

L15 ANSWER 8 OF 192 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

Full-text

ACCESSION NUMBER: 2001058475 EMBASE

TITLE: **Simvastatin** inhibits noradrenaline-induced hypertrophy of cultured neonatal rat **cardiomyocytes**.

AUTHOR: Luo J.-D.; Xie F.; Zhang W.-W.; Ma X.-D.; Guan J.-X.; Chen X.

CORPORATE SOURCE: J.-D. Luo, Department of Pharmacology, Guangzhou Medical College, Guangzhou 510182, China. joluoa@public.guangzhou.gd.cn

SOURCE: British Journal of Pharmacology, (2001) 132/1 (159-164). Refs: 22
ISSN: 0007-1188 CODEN: BJPCBM

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB 1. Oxidative mechanisms have been implicated in neonatal **cardiomyocyte** hypertrophy. We and others have shown that a HMG-CoA reductase inhibitor preserves endogenous antioxidant enzyme activity and inhibits cardiac hypertrophy in vivo. We therefore have examined whether noradrenaline (NA) induces the generation of reactive oxygen species (ROS) during its induction of neonatal **cardiomyocyte** hypertrophy and whether **simvastatin**, a HMG-CoA reductase inhibitor, attenuates ROS production and thus NA-induced hypertrophy of **cardiomyocytes**. 2. NA increased the intracellular ROS levels in a concentration-dependent manner. This increase of ROS was significantly inhibited by **simvastatin** and catalase. Prazosin partially suppressed NA-induced increase of ROS and beating, while preincubation with both prazosin and **propranolol** completely abolished NA-evoked increase of ROS and beating. **Simvastatin** did not affect NA-induced increase of beating. 3. The NA-induced increase of protein content was partially suppressed by prazosin and completely abolished by preincubation with both prazosin and **propranolol**. **Simvastatin** inhibited the increase of NA-induced increase of RNA content and [(3)H]-leucine incorporation in a concentration-dependent manner. Mevalonic acid (MVA) reversed the inhibition of NA-induced RNA and protein increase by **simvastatin**. Catalase also inhibited the NA-induced increase of RNA and protein. 4. We conclude that the inhibitory effects of **simvastatin** on myocyte hypertrophy were associated with its antioxidant effects and inhibition of MVA-metabolism pathway in neonatal rat **cardiomyocytes**. NA-induced increases of intracellular ROS and **cardiomyocyte** hypertrophy requires both α and β adrenoceptors activation in neonatal rat **cardiomyocytes**. The increases of ROS induced by NA is required for hypertrophy.

RN (**simvastatin**) 79902-63-9; (noradrenalin) 1407-84-7, 51-41-2; (catalase) 9001-05-2; (prazosin) 19216-56-9, 19237-84-4; (**propranolol**) 13013-17-7,

318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (RNA) 63231-63-0; (leucine) 61-90-5, 7005-03-0; (mevalonic acid) 150-97-0

L15 ANSWER 9 OF 192 DRUGU COPYRIGHT 2001 DERWENT INFORMATION LTD
Full-text
ACCESSION NUMBER: 2001-36589 DRUGU P S
TITLE: Colesevelam hydrochloride: a novel bile acid-binding resin.
AUTHOR: Aldridge M A; Ito M K
CORPORATE SOURCE: Univ.Pacific
LOCATION: Stockton; San Diego, Cal., USA
SOURCE: Ann.Pharmacother. (35, No. 7-8, 898-907, 2001) 1 Fig. 5 Tab. 37 Ref.
CODEN: APHRER ISSN: 1060-0280
AVAIL. OF DOC.: Department of Pharmacy (119), VA San Diego Health Care System, 3350 La Jolla Village Dr. 119, San Diego, CA 92161-0001, U.S.A. (M.K.I.). (e-mail: uopito@aol.com).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 2001-36589 DRUGU P S
AB The effects of colesevelam hydrochloride are reviewed. The pharmacology, phamacokinetic/pharmacodynamics, and clinical studies on colesevelam are discussed. Colesevelam monotherapy and combination therapy with **simvastatin**, **atorvastatin**, and **lovastatin** are considered. The safety profile of colesevelam and its drug interactions with digitalis, glycosides, digoxin, warfarin, valproic acid, quinidine, **metoprolol**, **lovastatin**, and verapamil are described. Therapeutic and economic issues and formulary recommendation on the use of colesevelam are explained. HMG-CoA reductase inhibitors are the drugs of choice for patients with primary hypercholesterolemia since these medications are the most efficacious in reducing LDL cholesterol, are well tolerated, and reduced **cardiovascular** morbidity and mortality.
ABEX Colesevelam has a high affinity to dihydroxy and trihydroxy bile acids in the intestine, which increases fecal bile acid secretion reducing the enterohepatic circulation of bile acids. Colesevelam has better bile acid-binding activity compared with currently available bile acid-binding resins. Mean maximum whole blood equivalent concentration of colesevelam is 0.17 ug Eq/ml at 72 hr after a dose. The peak effect of colesevelam occurs during the 1st 2 wk of therapy when LDL cholesterol concentrations drop rapidly. Combination therapy produces at least an additive effect over monotherapy with either colesevelam or **lovastatin**. Colesevelam plus **simvastatin** reduces LDL cholesterol and increases HDL cholesterol. Colesevelam plus **atorvastatin** is not different from **atorvastatin** (80 mg/day) in terms of percent change in LDL cholesterol. Colesevelam is well-tolerated, and does not change hematologic parameters, concentrations of vitamins E and A, partial thrombin or prothrombin time, estradiol concentrations, body weight, systolic, and diastolic B.P., or HR. Colesevelam has no effect on the bioavailability of digitalis, glycosides, warfarin, valproic acid, quinidine, **metoprolol**, and **lovastatin**. Digitalis, glycosides, warfarin, valproic acid, quinidine, **metoprolol** and **lovastatin** decrease the Cmax and AUC of sustained release verapamil by 31 and 11%, respectively. Colesevelam is 2-4 times more potent on a gram-to-gram basis than cholestyramine and colestipol. Colesevelam has a favourable pharmacokinetic profile and appears to have no effect on the bioavailability of digoxin, **lovastatin**, **metoprolol**, quinidine, valproic acid, and warfarin. (MLM/LL)

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AB Secondary prevention therapy in patients with coronary artery disease (CAD) is reviewed with reference to risk factor modification, **cardioprotective** drug therapy and myocardial revascularization. Risk factor modifications include lipid reductions, hypertension treatment, diabetes, hormone replacement therapy, cigarette smoking and exercise. **Cardioprotective** drug therapies include antiplatelet/anticoagulant agents (aspirin, ticlopidine, clopidogrel bisulfate, warfarin), beta blockers, ACE inhibitors, nitrates (isosorbide mononitrate), calcium channel blockers (diltiazem, verapamil) and vitamin E. Revascularization is achieved by percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass surgery (CABG). Secondary prevention by risk factor modification and by drugs established as **cardioprotective** is highly effective in reducing coronary events.

ABEX The cornerstone of lipid-lowering therapy is dietary modification which should be maintained even if antihyperlipidemic drugs are required. The most effective agents are the HMG CoA reductase inhibitors, or statins, which block the rate-limiting step in hepatic cholesterol synthesis. Such drugs include fluvastatin, **lovastatin**, pravastatin, **simvastatin**, **atorvastatin** and **cerivastatin**. Side-effects are relatively rare with these drugs. Estrogen replacement therapy in postmenopausal women augments HDL cholesterol, while greater increases have been achieved with gemfibrozil and nicotinic acid. Nicotinic acid, however, has been associated with side-effects, including flushing. The fibrate group, including gemfibrozil, clofibrate, bezafibrate and fenofibrate reduce triglycerides and LDL cholesterol and increase HDL cholesterol and are generally well tolerated. Cholestyramine and colestipol bind salts in the gut which leads to increased receptor-mediated uptake of LDL cholesterol from plasma. Both systolic and diastolic hypertension are risk factors for CAD. B.P. control can be achieved with numerous agents. Diabetes is another risk factor for CAD. Glycemic control is achieved through diet, exercise, oral hypoglycemic agents, insulin or combined drug therapy. Beta-blockers block beta-1 and beta-2 receptors in the heart, lung and peripheral vasculature and include **metoprolol**, **atenolol**, **propranolol**, nadolol, labetalol, sotalol and acebutolol. ACE inhibitors inhibit angiotensin-converting enzyme, thereby preventing the formation of angiotensin II, a potent vasoconstrictor. (E161/ECB)

CT CORONARY-DISEASE *TR; **CARDIOPATHY** *TR; ARTERIOSCLEROSIS *TR; VASCULAR-DISEASE *TR; IN-VIVO *FT; CASES *FT; REVIEW *FT; RISK-FACTOR *FT; LOW *FT; DENSITY *FT; HIGH *FT; LIPOPROTEIN. . .

CT CORONARY-DISEASE *TR; **CARDIOPATHY** *TR; ARTERIOSCLEROSIS *TR; VASCULAR-DISEASE *TR; IN-VIVO *FT; CASES *FT; REVIEW *FT; RISK-FACTOR *FT; LOW *FT; DENSITY *FT; HIGH *FT; LIPOPROTEIN. . .

[02] ASPIRIN *TR; TICLOPIDINE *TR; CLOPIDOGREL-BISULFATE *TR; WARFARIN *TR; ISOSORBIDE-MONONITRATE *TR; DILTIAZEM *TR; VERAPAMIL *TR; TOCOPHEROL *TR; FLUVASTATIN *TR; **LOVASTATIN** *TR; PRAVASTATIN *TR; **SIMVASTATIN** *TR; **ATORVASTATIN** *TR; **CERIVASTATIN** *TR; GEMFIBROZIL *TR; NICOTINATE *TR; CLOFIBRATE *TR; BEZAFIBRATE *TR; FENOFIBRATE *TR; COLESTYRAMINE *TR; COLESTIPOL *TR; INSULIN *TR; **METOPROLOL** *TR; **ATENOLOL** *TR; **PROPRANOLOL** *TR; NADOLOL *TR; LABETALOL *TR; SOTALOL *TR; ACEBUTOLOL *TR; CAPTOPRIL *TR; ENALAPRIL-MALEATE *TR; ENALAPRILAT *TR; RAMIPRIL *TR; TRANDOLAPRIL *TR; BENAZEPRIL. . . *FT

[03] ASPIRIN *AE; TICLOPIDINE *AE; CLOPIDOGREL-BISULFATE *AE; WARFARIN *AE; ISOSORBIDE-MONONITRATE *AE; DILTIAZEM *AE; VERAPAMIL *AE; TOCOPHEROL *AE; FLUVASTATIN *AE; **LOVASTATIN** *AE; PRAVASTATIN *AE; **SIMVASTATIN** *AE; **ATORVASTATIN** *AE; **CERIVASTATIN** *AE; GEMFIBROZIL *AE; NICOTINATE *AE; CLOFIBRATE *AE; BEZAFIBRATE *AE; FENOFIBRATE *AE; COLESTYRAMINE *AE; COLESTIPOL *AE; INSULIN *AE; **METOPROLOL** *AE; **ATENOLOL** *AE; **PROPRANOLOL** *AE; NADOLOL *AE; LABETALOL *AE; SOTALOL *AE; ACEBUTOLOL *AE; CAPTOPRIL *AE; ENALAPRIL-MALEATE *AE; ENALAPRILAT *AE; RAMIPRIL *AE; TRANDOLAPRIL *AE; BENAZEPRIL. . .

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